

WILLIAM V. MACFARLANE, M.B., Ch.B.,  
37 ARDEN STREET,  
EDINBURGH.

26th. MARCH, 1934.

VULVO-VAGINITIS DUE TO NEISSER'S DIPLOCOCCUS.

A TREATISE ON THE ABOVE SUBJECT WITH SPECIAL REFERENCE  
TO TREATMENT, BASED ON A SERIES OF CASES NUMBERING  
APPROXIMATELY ONE HUNDRED, AT THE EDINBURGH V.D. CLINIC  
FROM 1927 - 1933.



Gonorrhoea as a disease, has been known from the early annals of history, e.g. one sees it referred to in the Bible and the ancient medical works. Vulvo-Vaginitis however, does not appear until later, comparatively so, and one finds amongst the first articles on the subject, that of Suchard<sup>1</sup> in 1877 dealing with an epidemic at that time. From that period however, Vulvo-Vaginitis as a whole, gradually became universally recognised, workers in all parts of the world sought not only to discover the etiology of the disease, but also to exterminate it. "A new species of coccus specific for Gonorrhoea" i.e. Gonococcus by Neisser in 1879 naturally caused workers to turn their minds to this organism regarding the etiology of Vulvo-Vaginitis. Once interest was aroused, it was not long before others furnished cases illustrating that Vulvo-Vaginitis of Gonococcal origin existed in children e.g. De Minine<sup>2</sup> in 1895 described many cases due to sexual infection more so in the negro class: PRAT, VEIL and BAYON<sup>3</sup>, HAMILTON<sup>4</sup> amongst others also quoted numerous cases shortly after De Minine's time. Since then this disease, at times even a scourge, has attracted much attention, not so much from the etiological point of view but regarding treatment which will be dealt with in detail. As we stand at present Gonococcal Vulvo-Vaginitis presents one of the gravest social, as well as medical problems with which we have to contend.

Like every other known disease certain

facts are prominent, no matter from what angle one considers this condition. The infectivity, the intractability, the relative youth of the child among other factors create an indelible impression of the magnitude of the disease, with which one has to contend. One line of thought which can sum up more or less briefly the above facts, we shall consider:-



## I N C I D E N C E

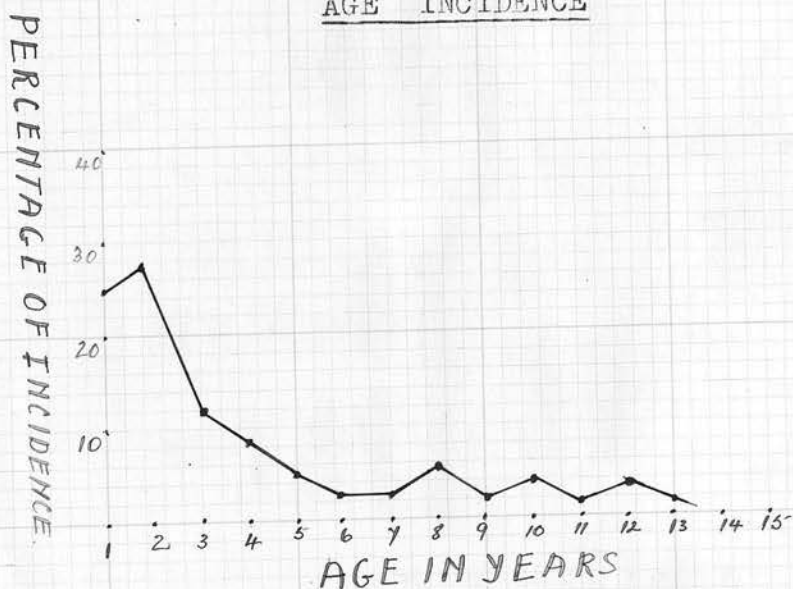
To simply enumerate a few statistics is rather misleading. One must qualify this by mentioning that figures vary with many factors of which one can mention a few of the more important.

(a) Social Conditions, Typical of most contagious diseases Gonococcal Vulvo-Vaginitis finds a high percentage of its cases in the poorer classes. Body resistance undoubtedly plays a part in fighting off the disease. The question of natural specific resistance will be referred to later (see General Discussion). Naturally a frail child won't combat the infection so well as a strongly built one. Other matters, however, such as Education both as regards habits pertaining to cleanliness and morals, enter into the question. A child brought up in an environment where cleanliness is of subsidiary importance is more fertile soil for the Gonococci to thrive in, than an otherwise clean child. Not only personal cleanliness but also that of the surroundings is important. This we shall refer to when discussing "Etiology". Likewise the morality of the child's cohabitants plays an equally important part e.g. Sexual assault.

(b) The Age Factor Age does seem to have a definite correlation to incidence in this disease. From the 100 odd cases investigated, we find the following:

Represented by Chart No.1.

CHART No 1  
showing  
AGE INCIDENCE



The maximum percentage of cases regarding age occurred around the 2nd year, the curve gradually falling from that figure 28.4% to the 7th. year where it rose from 3% to 7% in the 8th. followed one more by a general decline.

This more or less agrees with records published by other authors. For example Lees<sup>5</sup> in the same clinic for a period of 5 years (1922-27) found a gradual increase in incidence until the 5th. year of life followed by a gradual decline.

Below are the figures from various sources.

<u>1</u> <u>Brown</u> <sup>6</sup>	<u>2</u> <u>Lees</u>	<u>3</u> <u>Own Figures</u>
- 1 Yr. 4%	- 1 Yr. 7.4%	- 1 Yr. 4.2%
1 - 5 Yrs 54%	1 - 5 Yrs 39%	1 - 5 Yrs 69%
5 -10 " 31%	(3) - 10 " 44.9%	5 -10 " 20.8%
10 -12 " 10%	10 -15 " 8.4%	10 -12 " 5.9%

Buckley-Sharp<sup>7</sup> and Tod<sup>8</sup> likewise agree that the highest point in "the curve" is reached around the 5th. year. Our personal experience as the chart illustrates, was the higher incidence of cases in children a little under 5 years of age than over. This was more in keeping with Brunet's<sup>9</sup> figures where the percentage reached a little over 30% by the second year.

Why should this age harbour the highest percentage of cases? Tod explains it, by attributing handling of the young child as a more potent source of infection rather than any physiological reason (which will be discussed later), or otherwise. While there may be some truth in that, one can imagine other and more fruitful sources of infection playing a more prominent factor in the transmission and implanting of Gonococci in the Genitalia of the child. It has been noted repeatedly that boys of the same age, running the same risks (e.g. swimming baths) are much less susceptible. Does this not suggest the question of the anatomical factor as being important.

As regards the average age of Vulvo-Vaginitis child the following are quoted.

<u>Author.</u>	<u>Average Age</u>	<u>Range of Years.</u>
a.Brown	4.6. Yrs.	10/12 - 12
b.Reith Fraser <sup>10</sup>	4.7. "	9/12 - 12
c.Williams <sup>11</sup>	6.5. "	9/12 - 12
d.Titus & Notes <sup>12</sup>	12 "	7 - 14
e.Kurzwell & Saxl <sup>13</sup>	-	4 - 12
f.Hamilton <sup>4</sup>	5 "	3/53 - 12.5.

Our figures are lower regarding the average age, than any of the above - that being 3.9 years. Ofcourse, bearing in mind the high percentage of cases about 3 years of age this was bound to follow. The youngest case observed was that of an infant 12 days old - the oldest  $12\frac{1}{4}$  years. (The former was interesting, since Ophthalmia Neonatorum was also present. It is most likely the Vulvo-Vaginitis was the original source, since a gap of 12 days between the birth of the child and the occurrence of the eye complication is rather long). From one's own observations, one cannot agree with Buckley-Sharp "that the disease is rare under one year, unless in Hospital Epidemics".

#### SEASONAL INCIDENCE

This is discredited by many authors, but Buckley-Sharp has found cases to be most numerous in

the Autumn and least frequent in the Summer months because of the increase of adult cases during the Summer. Our personal observations do not agree with Sharp's - quite the contrary - the numbers being distributed equally throughout the year. One highly important factor which upsets the theory of Seasonal Incidence from the point of view of actual figures is that of

### EPIDEMICS

As already mentioned Suchard was one of the earliest authorities to publish literature on this question of Epidemic Vulvo-Vaginitis. Atkinson,<sup>14</sup> Skutsch,<sup>15</sup> Cotton,<sup>16</sup> Plomley<sup>17</sup> and Hurdon<sup>18</sup> amongst others also record epidemics of a similar type. Even at the present day, despite prophylactic as well as attempted curative measures, epidemics will and do occur. In our Centre in Edinburgh, epidemics occurring during 1927 and 1932 in certain Hospitals in the town augmented our numbers considerably in the series under review. In such cases, whether they arise in or out of Hospital, the disease runs amok and such factors as age, social surroundings, seasonal incidence etc. are subsidiary elements in the circumstances.

The incidence of Vulvo-Vaginitis shows a wide variation in different countries. Pollock<sup>19</sup> reveals the astounding figures from Baltimore that of the young females he examines annually, 800 - 1000 suffer

from Vulvo-Vaginitis. Ofcourse this condition is not due to Gonococci in every case. Dirt, Threadworms, B.Coli, Staphylococci, Streptococci, Diphtheroid Bacilli are often the causal factors in Non-Gonococcal cases. Buckley-Sharp found at Great Ormonde Street Hospital over a period of 11 years (1917 - 28) 20% of children examined for Vulvo-Vaginitis of Gonococcal origin were found positive. Other authorities give the following percentage of positive Gonococcal cases:-

a. Morrow & Bridgeman <sup>20</sup>	55% of girls entering a State Training School.
b. Watson <sup>21</sup>	2 - 12% of all children Hospital for routine Medical Examination.
c. Kidd & Simpson <sup>22</sup>	8% under similar circumstances.
d. Pott <sup>23</sup>	2.5% of all female children examined.
e. Kimball <sup>24</sup>	11.6% positive in cases admitted to Public Wards in Babies Hospitals in New York.
f. Reith Fraser <sup>25</sup>	63 such cases in General Practice.
g. Brown <sup>6</sup>	In reviewing case records at Guy's Hospital from 1925 - 1929, found the case incidence to be 12.5%, maintaining a more or less constant percentage each year - the ratio of Gonococci to non Gonococci being 1 - 1.5

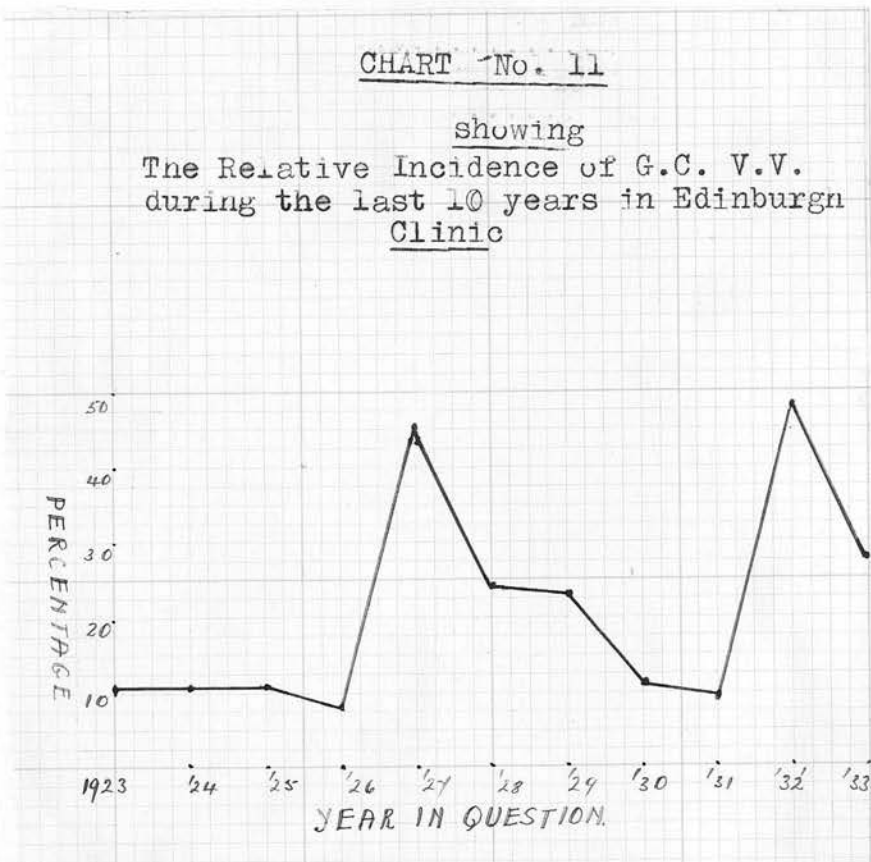
Paine is definitely of the opinion that less than 10% of Vulvo-Vaginitis are Gonococcal in origin.



The above figures have been quoted to illustrate the great diversity not only regarding incidence of Vulvo-Vaginitis but also of Gonococcal Vulvo-Vaginitis. Without entering into discussion, one would regard Paine's figures as being much below that of the others. One is more impressed with those of Brown, Kidd and Simpson, and Watson.

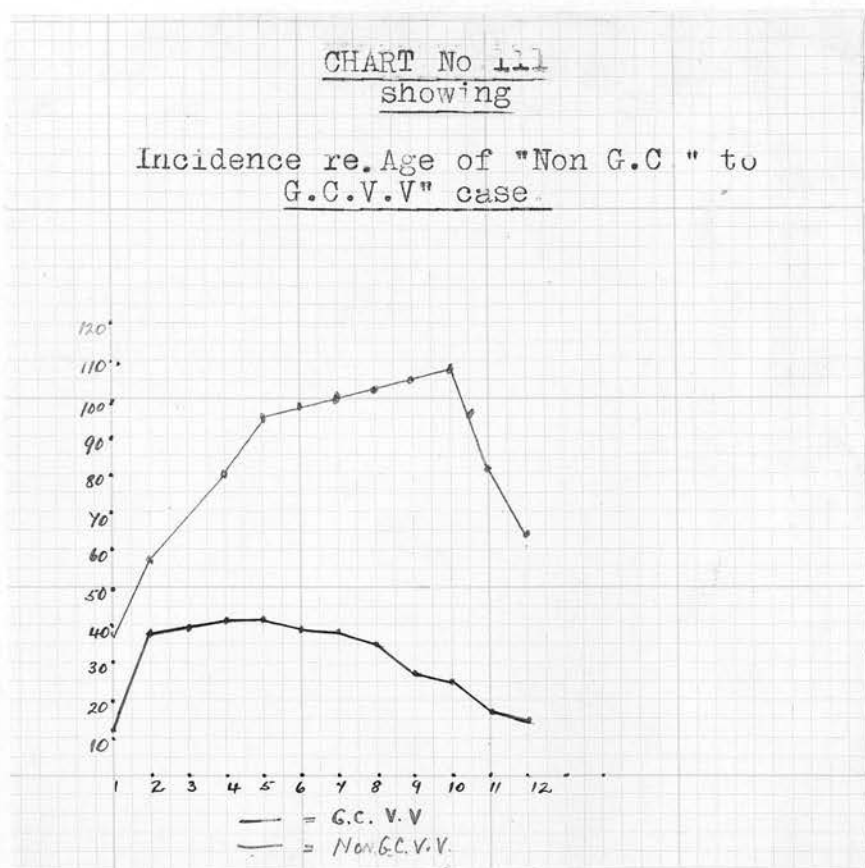
Working it on a percentage basis, the results regarding relative incidence which one has gathered in the Edinburgh V.D. Centre during the past 10 years are as follows.

CHART NO.11.



Thus one concludes from the above figures, that apart from those three epidemics the case incidence compared favourably with that of Brown's, namely 12% approximately. As we were dealing with Vulvo-Vaginitis only of Gonococcal origin, we cannot come to any definite conclusion on Buckley-Sharpe's observation—that the incidence of the disease, with regard to age, differed in those cases of Non-Gonococcal origin. This is illustrated in the following chart.

CHART No.111.





Such figures indicated that, according to Sharp's experience, Vulvo-Vaginitis of Gonococcal origin tends to occur earlier in life.

In conclusion from all that has already been said, one cannot fail to appreciate the fact that Gonococcal Vulvo-Vaginitis is very common, much more than one would expect.

ETIOLOGY OF VULVO - VAGINITIS

Quoting Lees, the following maxim sums up the question of the etiology of Vulvo-Vaginitis. "Every case of vulvar or vaginal discharge in a child must be regarded as Gonococcal until it is proved with certainty that the Gonococci are not present in the secretions when examined by direct film or by culture, or by both repeatedly, and that there is some other definite cause". 75% of cases of Vulvo-Vaginitis is due to Gonococci in the opinion of Abel.<sup>26</sup> Other figures, notably those of Dukelski<sup>27</sup> who places it at 80%, Plonley<sup>17</sup> 85.7%.; Spaulding<sup>28</sup> 68%; and Lees 99% in acute cases, show that the causal organism in by far the majority of cases is undoubtedly Gonococcal. This organism, easy to recognise in the acute case, is only too often missed. Naturally, it is extremely difficult to find in the less acute case, notably when secondary infection is present, which is the rule rather than the exception. Those difficulties will be referred to when the question of diagnosis is considered, but in passing Michelberg's<sup>29</sup> observation, that errors in morphological features, staining the film etc. render the process all the more difficult. In the absence of Gonococci the presence of other organisms raise the question as to whether they are the causal factor, or secondary to Gonococci. Repeated and careful examinations are essential, as Stein observes.

As already mentioned, other organisms may cause Vulvo-Vaginitis:- Streptococci, Staphylococci,

B. Coli, Pneumococci, Micrococcus, Catarrhalis (Smith),<sup>30.</sup>  
 Diplococci other than Neisser's (Fischer),<sup>31.</sup> B. Diphther-  
 iae, Vibrios and Spirochaetes of a certain variety<sup>32.</sup>  
 (Sherber), Vincent's Organisms, Dirt, Glycosuria,  
 Threadworms, Trauma, Masturbation attempts at coitus,  
 foreign body, lacerations, Tuberculous ulcerations,  
 Impetigo, mucoid excess at puberty, superficial  
 ulcers, pediculi, scabies, eczemas, Staphylococcal and  
 Streptococcal Skin lesions may also lead to a non -  
 Gonococcal Vulvo-Vaginitis. From those various  
 etiological factors, obviously one or more of the above  
 can favour or potentiate an already existing Gonococcal  
 infection also the

METHODS OF INFECTION need not be and  
 are not always the same in acquiring the infection, and  
 since it is with specific reference to Gonococcal  
 Vulvo-Vaginitis that we are concerned, it does not  
 require much imagination to understand the multipl-  
 icity of sources and ways leading to the acquiring  
 of the condition. Dealing with the sources of  
 Infection :- there is one outstanding fact; It  
 was impossible for us to discover in fully 40% of  
 cases the exact source. Once the source was dis-  
 covered one was not at such a loss to understand why  
 the child was infected. Admittedly one had not been  
 able to examine the parents of the child in 48% of  
 those cases where the source was not determined, but  
 even in those cases where the parents were examined

for Gonococcal Infection, the results were surprisingly disappointing regarding the percentage of Gonococcal positive cases, or even with a history of having had previous Gonococcal Infection.

Certain methods of acquiring the infection dispel the idea that Gonococci can live under very favourable conditions and for a very short time "in vitro". Swimming Baths, in particular, ever since Suchard's observation on an epidemic of Vulvo-Vaginitis due to this source, have attracted much attention and proved a frequent source of such epidemics. Engering showed that certain strains of Gonococci lived in tap water at a temperature of 22° Centigrade for 3 - 10 hours; in the surface water of swimming baths for 7 hours; in the deeper water of these baths for 8 - 14 hours; on moist linen for 4 hours; on dry linen  $\frac{1}{2}$  - 1 hour; on wet sponges 24 hours. Von Pourtales proved that Gonococci can be found on infected clothing after it is saturated with 25% lysol for 5 hours. Cultures at the end of that period were 10% positive.

Such striking facts explain the numerous sources of Gonococcal Vulvo-Vaginitis. Swimming baths, infected clothing, thermometers, baths, bed linen, towels, diapers, night clothing, sponges and in fact anything coming in contact with the Ano-Genital region in young girls or infants is a potential source. Epidemics have also been traced to lavatory seats.

This, in Taussig's opinion is the commonest source. In Institutions it is more or less always moist or likely to be more so than in private houses. Dryness is lethal to the Gonococcus, but the moist infected lavatory seat, proves a frequent method of infection. The young child is too small, and manoeuvring on the high lavatory seat may result in her smearing the genitalia with an infected drop of urine.

Precocious sexual intercourse, masturbation (through infected fingers of the child, say from an infected eye), "Breech presentations", rape, social hygiene (the sleeping of the child with an infected parent),<sup>36</sup> are all possible sources. Norris sums up the whole matter by saying "Gonococcal Vulvo-Vaginitis may be acquired by accidental infection, by the infectionist, by the sadist, by precocious sexual intercourse, and in rare instances by the passage of the child through an infected birth channel", especially, "Breech presentation" cases. As regards the question of Vulvo-Vaginitis being acquired during birth, Kidd and Simpson do not believe such a thing is possible.<sup>37</sup> Lees, Morton and others however maintain that it can and does exist, and they go further and show that this source has been reduced to a minimum as a result of the strict asepsis now observed during labour, and prophylaxis during pregnancy. Possibly this explains why Kidd and Simpson do not believe in its existence. To my knowledge none of our cases originated thus.

Different opinions prevail as to which is the commonest methods of acquiring the infection. Taussig, we have seen maintains the lavatory seat to be the most fruitful source of infection. Trenwith<sup>39</sup> found, he could trace most of his cases to an infected father; Buckley-Sharp says the source is directly or indirectly an infected adult. The following are a few of the figures quoted by different authorities.

<u>Author</u>	<u>Parents</u>	<u>SOURCES</u>		<u>Assault</u>	<u>Hospital Instit- utions</u>	<u>Un- known</u>
		<u>Lavatory Seat.</u>	<u>Other Sources</u>			
a.B.Sharp	20%	-	19%	-	11%	50%
b.Brown	42.5%	-	-	-	-	-
c.Lees	32%	-	-	-	-	-
d.Guy's Hospital	13%	-	-	4.3%	15.7%	67%
e.Childrens Medical Home	31%	-	-	11%	-	58%
f.Reith <sup>39</sup> Fraser	17%	5%	-	1%	-	43%

The above list is somewhat incomplete but from these figures, one cannot fail to be impressed with the high percentage of cases, the sources of which remain undiscovered. As already mentioned my figures too, were very high for this particular group and would have been much higher had it not been for a few epidemics of Gonococcal Vulvo-Vaginitis the sources of which were determined, one in particular

being an infected thermometer. Infected parents did not play such an important part in this series of cases under review. Hospitals and Institutions, especially for the poorer people, are undoubtedly very dangerous sources especially with an infected child in their midst. Little imagination is required to understand how in such circumstances the condition would spread among young girls living together. Anything from the thermometer to the bath water, could act as the intermediate factor in the transmission of the disease. One point emphasised by Reith Fraser deserves attention and that is the handling of infected genitalia by nurses while bathing, or dressing the child and thus transmitting of the disease. From personal experience, we can safely say that even although healthy young female children are present in Wards where cases of Gonococcal Vulvo-Vaginitis occur, with all the necessary precautions taken, the possibility of "Cross-Infection" can be eliminated. Naturally, if at all possible, it is desirable that "Infected" children should be treated in a separate ward from other young healthy females.

Assault, rape etc. did not figure in our cases very much. Precisely, 2 cases were all on record. Such a method of infection is uncommon in this country and even then only in the poorer classes - it is much commoner in America. The belief that contact with a virgin will cure a Gonococcal infected male adult, explains many



assault cases especially among the coloured races, according to Norris.

<sup>40</sup>  
Paine maintains that Gonococcal Vulvo-Vaginitis can only be acquired by sex contact and that all other supposed Gonococcal Vulvo-Vaginitis are of a different origin i.e. non Gonococcal. He says for example, that childish habits may result in the transmission of Micrococcus Catarrhalis from the nasal mucosa to the genitalia, setting up an inflammatory process closely simulating a Gonococcal Infection. This was not our personal experience as shown in the following experiment.

Eight more or less acute Vulvo-Vaginitis of presumably Gonococcal origin were selected at random, (Gonorrhoea having been diagnosed clinically and microscopically). Cultures were grown, after numerous failures and a Gram negative diplococcus was obtained with morphologically might be, Gonococcus, Micrococcus Catarrhalis, Meningococcus. Bio-chemical reaction - fermentation of various sugars - gave positive readings for Gonococci in 100% of cases and negative for Micrococcus Catarrhalis in 100% of cases. Naturally, from such a limited number of cases one cannot draw definite conclusions, but from personal experience one cannot agree with Paine regarding the possibility of Micrococcus Catarrhalis being the etiological factor in many cases, although, may be and exceptional one now and again - at the most.



ANATOMICAL AREAS INVOLVED

Vulvo-Vaginitis is a misnomer with regard to the sites of disease under discussion. The Urethra is involved to a varying extent, e.g. <sup>5</sup> Lees found only 1% of his cases which did not develop a Urethritis. Others again say that this figure is much too high - that it is difficult to swab the Urethra without incurring contamination from a Vagina pouring pus. Sharp's figures were 50% Gonococcal positive urethritis in his series of cases. This does not compare favourably with the series under review where Gonococcal Urethritis was present in 80% of the total. <sup>11</sup> Williams got 21% positive Urethral cases but never in girls under 6 years of age.

Briefly speaking, the Gonococcus can invade any part of the Uro-genital tract liable to become infected in the adult female. But while this is possible, it seldom occurs. Involvement of the Uterus, Tubes etc. have been known to occur, but the Gonococcus generally limits itself to the Genital tract below that area. Histological and Physiological reasons explain why. The immature labia are small, smooth, hairless and everted - a poor barrier to infection from without. The Vulvar and Vaginal Mucous surfaces are lined with columnar epithelium, which at any time offers a poor resistance to infection but especially here, where in the case of the Vulva, constant irritation by movements and

and handling of the parts by the young child, accentuate and encourage an already existing though "early" infection. The absence of Menstruation with its mechanical advantages (e.g. flushing out the vagina) besides possible others; the absence of Döderleins Bacillus which promotes a bacterial flora in the Vagina inhibitory to the existence of the Gonococcus likewise aid and abet the development of Gonococcal Vulvo-Vaginitis.

Nature however, has attempted after a fashion, to counteract all these disadvantages. The Hymen tends to act as a barrier to the spread of a Vaginitis; The Cervix shows a closed Os behind which is a very rudimentary canal; Bartholinian Glands are very immature, show no accessible way through which Gonococci may harbour there - the duct, like the Gland being in the developmental stage. Even then however, apart from Bartholinian Glands, which are practically never involved, nature's attempts to arrest the progress are unsuccessful and even sometimes a drawback. Admittedly, Gonococcal Infection is located in the early phase of the illness to the lower third of the Vagina but I have seen it spread beyond the Hymen upwards to involve the Vaginal Cervix and in these circumstances the Hymen was a decided handicap. Apart from rendering access to the Cervix difficult, it dammed back the discharge and in one particular case I was successful in obtaining Gonococci from the junction of the Vaginal Wall and Hymen.

Involvement of the Vaginal Cervix is more frequent than one would suspect: Our incidence was 17% - a surprisingly high figure, not quite in keeping with observations made by other authorities e.g. - certain American authors pointed this out and emphasised the importance of this both from the point of view regarding treatment and also ultimate prognosis. Likewise, Hiss<sup>41</sup>, Rubin and Leopold<sup>42</sup> pointed out the frequent involvement of the Cervix but they go further and say this site, apart from the acute and early part of the subacute phase of the illness, is the sole part of the Genital tract responsible for the persistence of infection - the Vagina having healed up. With this we cannot agree - invariably on every occasion we examined the Cervix by means of a suitable Urethroscope, since in the majority of cases the size of the Vagina would not admit a suitable apparatus for Cervical examination.- the Vagina especially the lower two thirds showed definite pathological changes and thus must share its part of the responsibility for "keeping up" the infection.

One had little experience with any cases where the infection had extended beyond the Vaginal Cervix.

Just as the Urethra is likely to become involved for anatomical reasons, the Rectum is also liable to infection. This complication occurred in 1% of our cases - a marked contrast to the figure (93.7%) obtained by Reith Fraser who regards this condition as part of the clinical picture - NOT a

complication. Furthermore, he obtained in 11% of cases, Gonococcal positive Rectal Smears where the Urethrae were negative for Gonococci. In our "Rectal" cases the Urethrae were all positive for Gonococci.

In conclusion, one may say that Gonococcal Infection in the young girls can involve any structure liable to infection in the adult female, but is usually limited to those areas discussed above.

P A T H O L O G YLITERATURE OF THE ABOVE SUBJECT

<sup>43</sup>Finger was one of the pioneers in investigating the pathology of the Gonococcal Infection on the urethral mucosa. Inoculating moribund patients with Gonococci he observed the different changes in the tissues which are detailed below. Possibly his observations were facilitated by the fact that the tissues were in a devitalised state. <sup>44</sup>Luys showed the susceptibility of the columnar epithelium.

<sup>45</sup>Jadassohn demonstrated that the storage of Gonococci in the Polymorph Neutrophils is most prominent in the superficial layers of the mucous membrane. Later Hiss Rubin, Leopold pointed out the frequency and importance of Cervical involvement in the young child.

Presumably Hiss did not take into consideration the fact that autopsy observations do not give a true picture of the disease, since features such as congestion tend to disappear. To Wertheim <sup>46</sup>and Schridde <sup>47</sup>especially we owe much of our knowledge pertaining to Gonococcal Infection of the uterus and its appendages.

The Gonococcus is an organism and, when introduced into the human body, is treated as such by the tissues. This manifests itself by the process known as inflammation.

As far as we are concerned with body tissues, that of prime importance is the mucous membrane of the urethra and the lower part of the Genital Tract and Rectum, and, as we have seen already, this mucosa comprises columnar epithelium we shall take the urethra as a typical example.

A Microscopic study of the urethra subjected to Gonococcal Infection.

In the early stage of the disease the inflammatory process is merely confined to the surface of the urethra i.e. during the incubation period which on an average is about 36 hours. The Gonococci however, thrive exceptionally well on this ideal medium, multiply rapidly, and soon find their way between the columnar cells and later into the sub-mucosal region where they are often found in chain formation. By this time however, the reaction has assumed such proportions as to demand serum being poured out into the tissues, and the migration of numerous pus cells (polymorph neutrophils) to the focus of infection. The columnar cells, subjected to the added strain of many leucocytes engorged with Gonococci plus the exudated of serum, become stripped off their basement membrane and hence further tissue destruction is apparent. As to whether the Gonococci are ingested by the leucocytes or not, is a debatable point, but if this were the case, why does substances introduced into the body to produce a leucocytosis not abbreviate the course of the disease? Apart from leucocytes, Gonococci are never found in other

types of cells such as Epithelial cells, Mast cells, Eosinophils. Likewise Gonococci never invade the capillaries. Often it would seem Gonococci are present in epithelial cells but intravital staining shows this not to be so.

And so the struggle goes on - ultimately the tissue resistance gains the upper hand and signs of embryonic cells - the future mucosa - appear. Those cells do not give rise to columnar epithelium however, but to stratified epithelium. Thus the new mucosa is stronger, thicker and less liable to become infected again. However, it has its disadvantages since irritation of fairly long standing may result in hyperplasia of this special tissue the upshot probably being one of the following:-

- (1) caruncle
- (2) papilloma
- (3) condyloma
- (4) glandular and mucous Polypi.

This not infrequently happens.

Again the newly formed epithelial cells may "go wrong" - absorption occurring and, in their place, fibroblasts are laid down resulting in fibrous tissue formation which may or may not lead to stricture formation but we did not come across any cases which suggested early or possible ultimate stricture formation. Such is much commoner in the longer, and therefore more susceptible male urethra.



## THE GENITAL TRACT

EXTERNAL GENITALIA Apart from excoriation, reddening etc., nothing is outstanding in the acute phase, but in the chronic stage the vulva may present a picture not unlike that in the pregnant female, - bluish, congested, succulent, and may be markedly hypertrophic. The lower part of the Vagina, naturally is involved before the upper third. Pathologically one may see changes varying in degree from the mild congested to the grossly ulcerated type.

The following is a suitable classification of Vaginitis.

- a. Congestive type where the mucosa is red, glistening, and oozing a sero purulent material. Later there is marked proliferation and desquamation of the lining epithelium - forming an adherent caseous and foetid coating over the mucosa.
- b. Granular type -(usually later in the disease) - A sequel to the congestive phase or may be granular from the outset - the vaginal mucosa being studded over with granulations thus giving it an irregular appearance.
- c. Membraneous or Diphtheroid Vaginitis is less likely to occur in the Gonococcal type of Vaginitis but may do so. A pseudo-membrane of lardaceous material adhering to the Vaginal Wall.

The cervix even in the acute phase may show reddening, small punctate haemorrhages, with occasionally a bead of pus protruding from the os which



again may be enlarged, soft and oedematous. Later ectropium or ulceration may be visible in the Vaginal Cervix. Cervical involvement leads to further involvement of the Posterior Fornix and upper part of Posterior Vaginal Wall. Furthermore, the presence of Glands in the cervix implies chronicity of the disease or obstinacy. From all these possible changes around the Glands the openings of the Gland Ducts may become blocked say due to overgrowth of new mucosa resulting in Nabothian follicle formation. Hiss goes so far as to suggest that a reddened cervix may be the only indication of Genital tract involvement in the later stages of the disease. He based his results on autopsy examinations.

We have had little experience with involvement of the Genital tract above that area. Possibly this may be due to the absence of menstruation, which always incurs the risk of upward spread of infection. Tubual and Peritoneal Involvement does ~~xxx~~ occur but the Pathological changes will not be described here since they are similar to Tuberculosis or any other infection involving those regions.

Pathological Involvement of the urethra and Cervix proved to be the ultimate drawbacks in the treatment of Gonococcal Vulv-Vaginitis.

#### RECTUM

The Pathological picture in the rectum

is similar to that in the Vagina but less severe. May be this is due to excessive numbers of other organisms since it has been shown that the presence of Koch-Weeks Bacillus in the conjunctival sac reduces the virulence of the Gonococcal Infection in that region.

In addition, the mucosa tends to be of the pavement type rather than columnar. The danger of fibrous tissue formation with the ever present possibility of stricture must be remembered and guarded against.

PERSONAL OBSERVATIONS

Two cases showed involvement of the Rectum in our series. Here the pathological picture showed nothing out of the ordinary - the infection being of a relatively mild nature and devoid of complications. Repeated proctoscopic showed that not only did the condition return to normal but remained as such.

The urethra, as already mentioned, showed infection in practically every case, but apart from the first week or two of the disease revealed little microscopic pathological change. Nor could we find any evidence of permanent damage although one or two showed a persistent pouting of the meatus.

Naturally the Vulva revealed gross changes in the acute stage but those were of a relatively transient nature - the conditions subsiding quickly. One cannot agree with Hiss and others the Cervix was involved early. Our opportunities to examine the Cervix in the acute stage of the disease were limited, but we concluded that Cervical involvement, when it did occur, was later in the disease.

Three of our Vaginitis showed a granular type, difficult to treat, and slow to improve. No pseudo-membraneous types were encountered. The posterior and upper part of the Vaginal Wall was not a common sight in the early stage of the disease, but relatively common later, for reasons already explained. Vaginal inflammation was general and improvement was also general i.e. no part of the Vaginal Wall healed before another area.

The cervical cases numbered 17% approximately. As previously mentioned they only manifested themselves towards the chronic stage. They were never severe - no Erosion or formation of Nabothian Follicles was observed, but the infection in this region was a protracted one, despite the apparently mild degree of inflammation.

Local Adenitis was observed in 60 per cent of cases. They disappeared quickly as the disease passed from the acute to the lesser acute phase under the influence of treatment. I have purposely omitted to describe Pathological pictures of complications elsewhere in the body since these were common to any type of Gonococcal Infection.

THE EXAMINATION OF THE CHILD.

A difficult enough procedure in the healthy child, but much worse in an actually infected Gonococcal Vulvo-Vaginitis case. This applies more so to the older girl and occasionally general anaesthesia is essential when she is examined for the first time. Without such, one must gain the child's confidence before examination and here a competent nurse is often successful where a medical man fails.

The detailed History of the case is essential and should be taken prior to examination. Especially should one note the facts pertaining to

- (1) the discharge (initial appearance, colour etc),
- (2) urinary symptoms (frequency, dysuria etc.),
- (3) Are there any other little girls in the Household?—  
if so, have they ever had a "Discharge" similar to this?,
- (4) The health of the Parents regarding Gonococcal Infection e.g. regarding the mother, did any of the children have "ophthalmia" at birth; and so on.

Naturally, tact must be employed and the parents or friends must not be led to suspect the possibility of the true condition.

In the case of a child the Lithotomy position is preferable to the Knee and Elbow posture. Note, on general examination, the general build of the patient for her years. Examine the skin in general for evidence of infection other than of Gonococcal origin and with particular reference to Syphilis.

Examination of the lower half of the Abdomen is usually of little help in this type of case. Also look for Inguinal Adenitis, present in our cases to the extent of 60% - mostly of a transient type however.

Having put the child in the lithotomy position the Examiner must seat himself accordingly, i.e. directly opposite the patient and examine the local parts in good light. This latter point would seem trivial but from personal experience, one can truthfully say that often important features, otherwise regarded as apparent details, are liable to be missed if lighting facilities are not all that is desirable.

Next carefully inspect the External Genitalia - noting the condition of the vulva with especial reference to the presence of discharge (colour, quantity, site i.e. urethral or vaginal) the presence or absence of oedema, excoriation, crusting etc. Then swab the External Genitalia with a Eusol soak - discharge oozing from the Vulvar cleft is useless since - (1) contaminated by surrounding structures - clothes etc. and (11) one cannot tell whether it is urethral or vaginal in origin,

Bartholinian's Glands, as previously alluded to, do not come into the clinical picture. The urethral orifice next commands attention - the labia majora having been separated with the thumb

and forefinger of the left hand, redness, ectropium and ofcourse discharge should all be looked for. Often a urethral discharge is elicited by milking the urethra through the anterior vaginal wall. This is done by introducing the gloved forefinger into the Vagina and gently stroking the finger along the anterior vaginal wall from above downwards. If a Vaginal Smear is to be taken, which is very likely, do not insert the gloved finger into the Vagina until a smear has been taken from the latter. Separate the lips of the meatus and note the condition of Skene's Ducts as they pass forward in the roof of the urethra to open inside or just outside the meatus. A Loopful of the discharge is next taken from the urethra - the area around the meatus having been cleansed.

If a Vaginal Smear is to be taken, which is usual in a case being examined for the first time, one inserts a "dressed" Playfair Probe and rotates it in the Vaginal cavity. A speculum (of the bivalve type) is introduced into the vagina where possible, or in the case of a younger child and especially at the first "sitting", Harrison's Endoscope may be employed. (N.B. In passing the speculum care should be taken not to rupture the Hymen). The vagina having been cleaned up, one looks for areas of erosion, oedematous or inflamed patches, Infiltrated areas, inflamed crypts and crevices should also be noted. The Cervix having been swabbed and examined for changes similar to those found in the vagina should next be "smeared" - care being taken to obtain the

specimen from the "interior" of the Cervix - following which topical applications may be applied.

The Vagina even in the young child behind the Hymen is spacious and a speculum with the expanding type with internal illumination after the style of Sheaff is extremely useful.

Finally one should note the optimum time for taking "smears" is, when the child has not urinated for a considerable period. Naturally this is difficult where "frequency" is often a symptom. Likewise no local treatment should have been applied to the Vagina or Cervix for some time prior to taking Smear(s).

#### The Rectum

when involved may draw one's attention by reason of one or more of the following signs.

- (1) The drop - Brownish Fluid
- (2) Anal fissure
- (3) Condyloma - often smooth, moist, glistening.

All previously mentioned.

Proctoscopic Examination - will reveal a varying degree of Inflammation (usually mild) of the Mucosa. Personal experience showed only a slight superficial Rectal Mucosal Inflammation to be present in our cases.



C L I N I C A L   P I C T U R EGENERAL

Since this disease is commoner by far among the poorer classes the patient is usually under-size and thin for her years. Occasionally the child is perfectly healthy to look at. The disease itself manifests few systemic features (apart perhaps from the initial and acute stage when the child may experience feverish symptoms), since it is the exception rather than the rule for the disease to spread beyond the Vaginal Cervix. (In 2.7% of our cases we did notice Tubal and (or) Peritoneal Involvement but at a later stage in the disease. Even then however, the duration of complication which was of a relatively subdued nature was comparatively short.

So that from the clinical point of view acute cases should offer little difficulty. But one must bear in mind that young girl may have a purulent discharge with scarcely a complaint. Also the absence of discharge does not mean freedom from infection e.g. one found that 48.7% of cases were cured clinically before bacteriological examination indicated freedom from infection. It is remarkable how little a "Gonococcal child" may suffer and yet have relatively severe signs. Certain authorities regard this as being more typical of the older girl say about 10 or 12 years of age. With that one cannot agree, as many of our cases showing few symptoms and fairly severe signs were infants. Having had no experience



regarding the clinical aspect of Gonococcal Vulv-Vaginitis spreading beyond the cervix, one cannot deal with that matter apart from saying that in the young girl it is uncommon.

### LOCAL

The child may exhibit symptoms of a severe type, or none at all. An acute case usually commences with the child complaining of itching, localised pain, and a sensation of heat at the Vulvar orifice. This is aggravated by friction of the clothes rubbing on the parts, attempts at walking, etc. In our cases the vast majority complained of urinary symptoms, with special reference to frequency, dysuria and occasionally urgency. (Two cases of the latter type, had a "Trigone infection" of the bladder due to a secondary infection superimposed on the original one.)

If the process is even more severe, pain may be of such a severe scalding nature that voluntary retention of the urine results. Such is not common however, and one was fortunate enough not to experience this difficulty.

On Examination of the Parts involved, one notices usually oedema of the Vulva with excoriation around the vulvar region and inner aspects of the thighs; if the skin is dirty and the discharge is purulent, crusts may be observed in this area, ulcers, and even suppurating scratches, also bleeding surfaces

from denuded epithelial areas; Condylomata Acumenata. A discharge of varying intensity i.e. from Purulent to mucoid is usually present. It may be oozing from the anterior and of the vulva, or merely sealing the lips of the labia together.

Such a discharge is found also at the meatal orifice where the infection may be of such a severe nature as to cause everting of the meatal lips. Also the orifice of the hymen may show this discharge, and frequently one has found that the hymen dams back the discharged from the Vaginal surface. How much this increases the virulence or maintains the duration of the infection on the Vaginal Wall is difficult to say.

The cervix too may be involved at this early stage, but from personal experience one can say that to examine the cervix in a young acute Vulvo-Vaginitis is a well nigh impossible procedure without a General Anaesthetic.

The superficial Inguinal Glands often show an enlargement to a slight degree usually of a short duration. This however, was not present in 40% of our cases, and when present, the child never had symptoms referable to that area.

Tenesmus figured as a symptom in quite a few cases. Strangely enough, those two cases with Rectal Infection did not complain of this sign, but one or two of the older cases with the straight forward

Gonococcal Vulvo-Vaginitis complained of it, presumably a referred pain. Rectal infection may be present without any symptoms and comparatively little to show on examination. Occasionally, a drop of discharge from the anal region, a small fissure situated at the Posterior end of the anal orifice, or a condyloma, single, prominent, elongated, shiny, soft and almost painless - the most characteristic sign of amo-rectal Gonorrhoea - may lead you to suspect the presence of this condition.

On an average, the acute stage is passed in 21 days - the inflammation has subsided and apart from a certain amount of reddening of the parts there is little to be seen. Only too often, that is the time when one sees the case for the first time. A watery like discharge replaces the purulent type, and here one is often misled by its appearance. Repeated smears may show up Gonococci; failing direct smear examination cultural methods, in the hands of an expert often detect the presence of Gonococci. Intermittent dysuria or perhaps irritation due to the leucorrhoea, may be the only symptoms. In cases where vigorous methods of treatment have been employed during the acute stage the watery Vaginal discharge may persist for no apparent reason. Bacteriological Examination often failed to reveal organisms of any kind and one found that reduction in the strength of the irrigation antiseptic and frequency of irrigation often cleaned up the condition i.e. the child was suffering from

chemical irritation.

Again a child may be brought for Medical Examination with a history that the mother noticed staining of the child's clothing. This is the dangerous type of case - where the patient suffers little if any, yet shows Gonococci in the discharge - Typically a carrier of the disease. Eight cases of the total under review were brought to medical notice in this manner.

Among less common features is that referred to by Hamilton,<sup>48</sup> who found Nocturnal Enuresis in 2.9% of his cases. Such is an interesting observation as probably in fair percentages of children suffering from this complaint, closer examination might reveal a few cases with, or having had, Gonococcal Vulve-Vaginitis. Personally speaking one cannot give any opinion on this. Nocturnal Enuresis did occur in an occasional case but there it was difficult to assess the importance of Gonococci as the true etiological factor in the condition, as practically all the children with that complaint were fairly young.

## DIAGNOSIS

For convenience sake I shall classify this into certain sections.

### A. CLINICAL EXAMINATION

The History (gleaned from the relatives) of the case, is always valuable and especially so where the diagnosis of the disease is obscure e.g. in the more chronic type of case, or again where the source of infection is derived as a result of sleeping with an infected parent. Likewise a previous history of Infectious Disease or an Oxyuris infection of the bowel may make one suspicious, as to either of those being the etiological factor of the Vulvo Vaginitis quite independent of Gonococcal Infection. Again a case occurring during an epidemic of Vulvo Vaginitis is more likely to be of a Gonococcal origin as <sup>49</sup> emphasised by Baer.

Information obtained from the child does not play such an important part in this disease, since the child is usually too young to be of much help regarding its complaint, but occasionally, and especially so in older children, they may complain of symptoms leading to a diagnosis of the condition :- e.g. in chronic cases - dysuria and local irritation may lead one to suspect the condition.

So that, in the majority of cases, one must trust to ones power of observation. Inspection of the parts may give some valuable clues. Thus in

the acute case excoriation and signs of irritation of the external genitalia are often present. A purulent discharge - yellowish green and sometimes bloodstained - may be noticed at the anterior end of the Vulva cleft. More chronic cases may reveal no obvious discharge, but on attempting to separate the Labia one may find them adherent to one another due to a perhaps watery, thin and tenacious discharge.

Having invested the external genitalia, next examine the condition of the meatal orifice for signs, similar to those found in the Vulva. Assuming the diagnosis is still undecided e.g. in the more chronic case examination of the Cervix may be of value. Such a procedure is facilitated by employing Harrison's endoscope to show up the source of infection. (Naturally one notes the condition of the Vagina prior to examination of the Cervix).

Abdominal Examination (especially Palpation) was carried out in every case without yielding any information; Bimanual Examination only in the older cases, and it too yielded no useful help in the majority of cases.

And lastly, examination of the Rectum should never be omitted. Such may lead to the detecting of the presence of an Oxyuris Infection. One must admit that this was not suspected in one of the cases in this series, for a few days after Vulvo Vaginitis had been diagnosed. This was a case

of assault, and only when the History was ascertained plus the observation that the child complained of Anal irritation did one suspect the condition, (an illustration of the value of caseHistory). From the above, then, one cannot but fail to observe the necessity for further examination of the case. Lees and Buckley-Sharp maintain that acute cases can be diagnosed clinically. This too was our experience and was proved up to the hilt in four cases where clinical examination led to the diagnosis of the condition (i.e. Gonococcal Vulvo-Vaginitis) before:-

#### B. BACTERIOLOGICAL EXAMINATION.

This is an extremely important procedure in the diagnosis. Occassionally it may give little help, especially in the chronic stage of the disease but more often it is a valuable aid.

Lees<sup>5</sup> stressed the importance of Bacteriological examination by saying "Every Vaginal discharge occurring in children should be viewed with suspicion, and treated as if of Gonorrhoeal origin, until at least three bacteriological tests have been performed, under conditions favourable for the detection of the Gonococcus, and all prove Negative". In other words one negative examination does not rule out the possibility of Gonococci being present.



METHODS EMPLOYED TO DEMONSTRATE THE PRESENCE OFGONOCOCCI1. Microscopic Examination.

From personal experience one can truthfully say this is a source of pitfalls to the inexperienced. The technique employed in taking smears - especially from the Cervix; -the distortion of the Gonococci - possibly due to fixing the smear to the slide by heating, or again by staining i.e. imperfect morphologically due to mechanical interference; the imperfect decolorisation of the Gonococci, or again partial decolorisation of Gram positive organisms i.e. imperfect tinctorially; typical forms of Gonococci for example in the early immature Gonococci shortly after fission where they may be round or ovoid; the relative position they bear to the pus cells if any of the latter are present; the coexistence of Gonococci with other organisms with possibly the latter easily predominating.

All contribute to errors in all the diagnosis microscopically. Further the importance of the stain employed should be borne in mind. Never diagnose Gonococci on a "simple" stain such as Methylene Blue. One must decolorise to ascertain whether the organism is Gram Positive or Gram negative. Furthermore, one is apt to diagnose the presence of Gonococci when they actually are not present, on the strength of a previous positive or doubtful positive report.

In the very early stage of the infection the Gonococci are extracellular but soon become intracellular - their characteristic position - occurring in pairs with their concave aspect towards one another. Here however, owing to excess of numbers intracellularly they are apt to lose their typical shape and become, may be ovoid or round. Later on, the presence of other organisms (secondary infection) obscures the presence of Gonococci to a varying extent and finally in the chronic stage they may "cut out" the Gonococci completely. Therefore, who can say that organisms of the Streptococcal, Diphtheroid, Staphylococcal types may not be secondary to a Gonococcal infection although microscopically there is now no evidence of the latter? It has been said that a symbiosis of Diphtheroid Bacilli and Staphylococci warrants a further search for Neisser's Diplococcus. Again, a Bacteriological examination may reveal why a case is running an atypical course e.g. a predominance of secondary infection over the original Gonococcal infection can and does modify the course of the disease. For this reason the growing on culture of Gonococci under the circumstances is rendered difficult.

It has already been emphasised that a negative examination does not rule out the presence of Gonococci. Repeated examination is necessary, Thus Brown found that examination of the smears were positive for Gonococci in 61% of cases at their first visit and the remaining 39% later became positive.

In our series, we found that 82% were positive for Gonococci at the first examination, the remaining 18% ultimately becoming positive. Probably the reason for our finding such a high percentage of positives at the first examination was due to the fact that most of the cases were seen during the acute stage.

The importance of diagnosing Gonococci in Vulvo Vaginitis has already been emphasised but, in addition, certain authorities regard Non Gonococcal Vulvo-Vaginitis as an autoinfection in which case, isolation, quarantine and exclusion from school etc., are not essential.

In acute cases clinical and microscopic findings may be all that is necessary, but in more obscure cases one should resort to

#### 11. Cultural Methods.

<sup>50</sup>Anderson, Schultz, and Stein found in their series of cases 35.7% gave typical Gonococcal smears; 19% of the total gave positive Gonococcal cultures; 53.5% of the positive smears gave Gonococcal cultures. They concluded, where Gonococci predominated in the smears, the percentage of Gonococcal cultures was much higher (53.5%) as compared with the mixed smear which only yielded 19% Gonococcal positive cultures. While more modern methods would yield higher figures they are approximately, relatively the same.

"

Williams found that, where the smear revealed no Gonococci neither did the culture, and even with regard to cases showing positive smears only 50% gave a positive culture. His conclusions regarding the value of cultures as an aid to diagnosis are, that they are useless. Stein share this view also.

Brunet while not sharing the same pessimistic view found that only occasionally did a culture reveal Gonococcal colonies where smears were negative.

From the limited number of cases tried out we have experienced disappointing results. Doubtless much depends on (1) the medium employed, (2) temperature of the medium, (3) technique of taking the specimen, (4) care exercised in isolating Gonococcal colonies which at times were almost "overgrown" by other organisms.

Ellison's blood serum agar medium has been found much more satisfactory than Thomson's, since Gonococci were grown in the former where Thomson's medium failed. Ordinary Gland agar, one found to be very satisfactory. In taking the specimen of material all aseptic precautions must be taken - the "loop" only touching the area in question and the material must be transferred immediately to the medium which must be at a temperature of 37° C. Failure to appreciate this, results in cultures devoid of Gonococcal colonies.

Despite all those precautions, as I say, the results were disappointing. Actually from the number of cases we attempted to "Culture", 3% yielded Gonococci as compared with 82% positive Gonococcal diagnosis at the first microscopic examination. So that unless facilities are available, diagnosis by culture is a difficult and disappointing procedure. (In passing one may add that specimens from 22 cases sent to the Laboratory of the Edinburgh Royal Infirmary for the diagnosis of Gonococci by cultural methods in adult cases, NOT ONE has been returned "positive". In every case Gonococci were diagnosed microscopically).

If one is so fortunate to obtain a good growth of organisms simulating Gonococci then accurate diagnosis is forthcoming. Thus:-

- (1). The rate of growth of the organism on the culture may be helpful e.g. Micrococcus Catarrhalis grows much faster than Gonococci or Meningococci, while the latter grows less profusely than Micrococcus Catarrhalis but more so than Gonococci.
- (2). The colony, with concentric and radial striations plus scalloped margin is entirely different from that of Micrococcus Catarrhalis which is a raised, well defined border, and beaded aspect. Again the former differs from Meningococcus which tends to be flat with an ill defined border. as compared with the scalloped yet well defined border of the Gonococcal colony.

- (3) Fermentation and Sugar Reaction also aid in the differential diagnosis of Gonococci and Micrococcus Catarrhalis and Meningococcus thus:-

<u>Organism</u>	<u>Maltose</u>	<u>Glucose</u>
Gonococci	—	⊥
Meningococcus	—	—
Micrococcus Catarrhalis	⊥	—
⊥ = Fermentation;	— =	No fermentation,

### III. Opsonic Index and Cuti Reaction.

With regard to those measures as an aid to the diagnosis, I have had no experience, but the general consensus of opinion seems, that they are of little value.

### IV. Methods of Stimulating Latent Foci of Gonococcal Infection.

#### (a) Chemical Irritants.

Again I have had little experience in this line of diagnosis. It would seem that with the advent of Vaccines this method is much less used than formerly. Only in three cases was it attempted (1-2 % solution of Silver Nitrate being used) and our results were - no Gonococci found but the children in question suffered increased irritation and discomfort.

#### (b) Vaccines.

Similarly Vaccines failed in those three cases in question to reveal the presence of Gonococci. Vaccines, as will be discussed later, were employed

as a therapeutic measure rather than a diagnostic one. With regard to the dose of Vaccine employed as a diagnostic or provocative measure, one administered three millions of the Polyvalent type to a child aged 10 years - the dosage naturally varying in accordance with the age of the child. Smears were taken 24 - 48 hours after administration of the Vaccine from the sites of infection in question; usually the Urethra and Cervix, and often the Vagina itself.

(c) <sup>51</sup> Pribram and Jonas,

found that in early chronic cases, where cultures and smears were negative for Gonococci, that the application of fresh animal serum to a probable site of hidden Gonococcal infection was often successful in "bringing out" the Gonococci. Unfortunately, we had only the opportunity of employing this method on two occasions. The results were disappointing (no Gonococci being found) but one should add that this was probably due to us using a mixture of two human sera - no fresh animal serum being available. Such a method as suggested by those authors might be well worth a trial as in chronic Vulvo-Vaginitis cases the Cervix (which was the source of trouble in many of our cases and to which the mixture of sera was applied in the two cases already referred to), is very often the bugbear, being very difficult to clear up.

#### V. The Vaginal Secretion and its Reaction.



Buckley-Sharp has reported interesting results with regard to the Vaginal secretion in girls under the age of puberty, and its relation to Gonococci. Normally in young girls, before puberty, the Vaginal secretion is alkaline in reaction. With the advent of Döderlein's Bacillus the reaction becomes acid. He investigated several cases of young girls whose ages ranged from 11 weeks to  $4\frac{1}{2}$  years. Those with an alkaline reaction often harbour the organisms of a Gram positive or a Gram negative nature or perhaps both, plus a few leucocytes. He also found a purulent discharge gave an alkaline reaction but as soon as the discharge ceased the reaction became acid. Once cure was attained, back went the reaction to alkaline.

So that he concluded, in a patient who was infected and had been on treatment, stopped treatment, and the reaction was persistently acid then the patient was not cured despite her negative tests, and relapse was likely to follow. However, the converse does not hold good. Alkalinity does not always mean cure in the absence of a discharge. In 55 cases he got no acid reaction in cases of cure. Ofcourse, as already mentioned, the reaction alters as the girl approaches puberty.

In a small series of cases investigated on this point, one was forced to admit that the above statement was wonderfully accurate; only, in patients where Diphtheroid infection predominated the reaction remained strongly acid. Hence one was unable to derive much value from this test in the diagnosis or tests for cure in Gonococcal cases having a superimposed Diphtheroid infection.

## CONCLUSIONS

In the acute stage of the disease, seldom does one have to resort to methods other than clinical and microscopic examination to arrive at a diagnosis. Unfortunately however, too often does one see a case rather of the chronic type where Gonococci are extremely difficult to find. <sup>52</sup> Clauberg states that out of 4,500 children examined in the Berlin Orphan Asylum 10 - 20% showed a Vaginal discharge, but only in .1 - .3%, could one demonstrate the presence of Gonococci. Such figures at the present time would be open to criticism, since with present day facilities far more accurate examination and diagnosis would lead to a higher incidence of positive Gonococcal cases. The fact remains however, that even at the present time the percentage of cases actually diagnosed as Gonococcal is still too low. Whether it is, that the cases are not seen early enough in the disease, or whether the method of diagnosis at our disposal is still inadequate, is doubtful.

<sup>53</sup> Since the time of Muller and Oppenheimer, who were the first to investigate the blood as a means of diagnosing the presence of Gonococci, a vast amount of research has been carried out culminating in the

### VI GONOCOCCAL COMPLEMENT FIXATION TEST.

to which we shall now refer both from the diagnostic and prognostic points of view.

Diagnostic

This test is undoubtedly a valuable aid in the diagnosis of Gonorrhoea in general, provided it is applied with judgement. With special reference to Gonococcal Vulvo-Vaginitis however, its value is somewhat more limited. <sup>54</sup> Osmond and Oliver came to the following conclusions: - a very low percentage of wrong results (.6%) and 99% of correct results, in those cases especially with complications. Following clinical cure the change from positive to negative in the Gonococcal Complement Fixation Test takes a considerable time. Brown quotes the following figures:-

	<u>Gonococcal Complement Fixation Test.</u>	<u>Films regarding presence of Gonococci.</u>
a. 63%	+++	+ <sup>we</sup>
b. 16%	+	+ <sup>we</sup>
c. 21%	-	+ <sup>we</sup> in 50% of this group.

She concludes that a strong positive reaction was not present until four weeks after acquiring the infection. This does not belittle the test during this period from the diagnostic point of view, since films from those cases showed Gonococci to be present. Note that there was no false positives during this period. She also found the test valuable in detecting cases with hidden foci of infection.

Our experience on this subject is rather limited. Approximately 70% of cases had the Gonococcal Complement Fixation Test performed and



and results obtained were as follows:

<u>G.C.F.T.</u>	<u>"Smears"</u>	<u>Clinical Condition</u>
a. 13% <del>+++</del>	<del>+</del> (positive)	Fair
b. 11% <del>+</del>	<del>+</del> in 60% of those cases	Excellent
c. 46% <del>-</del>	<del>+</del>	Fair to excellent.

Thus we did not benefit much from this test as an aid to diagnosis. Probably this was because, we were fortunate in obtaining the cases at a time when Gonococci could be diagnosed microscopically without much difficulty. This applies especially to group "c". Only in a few cases in group "b" did one derive much help where Gonococci could not be found and this helped a little towards establishing the diagnosis.

Probable explanations why Group "c" was such a failure.

The lesion in children is a superficial one, i.e. mainly mucosal, where antibody formation in the serum as a result of local reaction is very limited. The more the Gonococci burrow into the Submucosal region the better chance of obtaining a positive reaction with the Gonococcal Complement Fixation Test. This probably explains to a large extent why in the first 3 - 4 weeks the vast majority of known Gonococcal cases give a negative result with the Gonococcal Complement Fixation Test, Anderson and Stein maintain there are different strains of Gonococci but they could not specify such-and-such

a strain for adults or children as the case might be.  
<sup>55</sup> Torry and Buckell say that there are not different strains for adults and children otherwise how can one get cases of Gonococcal Vulvo-Vaginitis originating from an infected parent. <sup>56</sup> Pearce supports Anderson and Stein, and maintains they can easily be identified by agglutination methods. On this basis he found the strains of Gonococci occurring in Ophthalmia Neonatorum to belong to the adult type. If such is the case, then the antigen employed in the test must need be a Polyvalent one as opposed to that prepared from one strain of Gonococci. This may to a certain extent explain in the less acute case, the failure to diagnose Gonococcal infection by means of this test, since it is obvious an antigen derived from Strain "A" is not going to produce agglutination (i.e. a positive result) in a person suffering from Gonococcal Infection of the Strain "B" type.

Micrococcus Catarrhalis and Meningococcus simulate Gonococci very closely in many respects, but have never been found to give a STRONG positive reaction, and with modern methods of preparing the antigen, false positives (due to these organisms) are fast disappearing.

Therefore, from personal observations:-  
 the Gonococcal Complement Fixation Test has a definite place in the diagnosis of Gonococcal Vulvo-Vaginitis but too much must not be expected from it. Acute

and early subacute stages are not satisfactory cases to diagnose by this method. Using the proper antigen (and especially polyvalent) the percentage of error would seem to be extremely low. Its great value lies in the more chronic or latent case where other methods have failed to label the Vulvo-Vaginitis as being of Gonococcal origin. The presence of complications (not usual in Gonococcal Vulvo-Vaginitis), tends to give an earlier and stronger positive reaction. And finally, drawing a parallelism between the Gonococcal Complement Fixation Test with regard to Gonococcal Vulvo-Vaginitis, and the Wassermann Reaction with regard to the diagnosis of obscure Syphilis, and while recognising that it would not be absolutely conclusive if negative, might one suggest the repetition of the Gonococcal Complement Fixation Test in doubtful or negative cases where one suspects for other reasons the presence of Gonococci. Admittedly, we do not derive the same advantages from the Gonococcal Complement Fixation Test in the early stages of the infection, as compared with the Wassermann Reaction but to make up for this defect we have microscopic evidence of the Gonococci being present.

D I F F E R E N T I A L     D I A G N O S I S .

In our experience, by far the most difficult question was the determining as to whether the Disease was of Gonococcal origin, or due to other Bacteria. Since the majority of cases were more or less acute the Gonococci were isolated without difficulty. But a small percentage gave not a little trouble, and in those cases, the procedure outlined in the section dealing with "Diagnosis", was employed. Even then one could not be absolutely certain.

Undoubtedly those organisms belonging to the same group as Gonococci were the stumbling blocks, especially Micrococcus Catarrhalis and to a lesser degree Meningococcus. The latter can occur in the urine and genital tract quite apart from Cerebro-Spinal Fever. Micrococcus Catarrhalis however, occurred more frequently, and was diagnosed along the lines already mentioned (i.e. Biochemical Reactions also evidence of infection in Naso-Pharyngeal tract etc).

Other organisms, less difficult to identify and more frequent, also presented difficulties, chiefly from the point of view as to whether they were the causal organism of the condition or secondary to the Gonococci - such organisms have been enumerated elsewhere.

Worms, and especially Oxyuris vermicularis, are a very frequent source of error in the diagnosis.



Occurring usually in large numbers, they cause general as well as local symptoms e.g. chronic Indigestion, reflex nervous symptoms (irritability, sleeplessness) etc. Itching leads to fingering of the infected parts thus facilitating transmission to the Genital region.

Therefore, one should never neglect to examine the rectum and contents in a case suffering from Vulvo-Vaginitis.

Certain Infectious Diseases may also cause this condition;

a. Scarlet Fever - where Vulvo-Vaginitis occurs as a complication and, if not suspected as such, may cause grave anxiety to the Hospital Staff, especially if such a case occurs in a ward occupied by other young females.

b. Diphtheria - again as a complication with a typical Diphtheroid membrane on the Vulva from which B Diphtheriae is often isolated.

c. Pneumonia - there the clinical picture may be identical with that of Gonococcal origin. Moreover, if the little patient has recovered from Pneumonia, this organism may be regarded usually in a saprophytic light, rather than pathogenic i.e. occurring in the Genital region.

#### Other Causal Factors in Vulvo-Vaginitis

The disease may be found in debilitated children of the poorer classes where cleanliness is

ignored i.e. a Simple Catarrhal Vulvo-Vaginitis.

Likewise in such classes one may find a Furunculosis involving this part of the body.

Trauma (e.g.) sexual outrages, foreign bodies) may also produce the disease but here the question of associated secondary infection must be considered.

Glycosuria, resulting from Urine frequently passed, and loaded with sugar as in Diabetes Mellitus may lead to severe irritation with or without a super-imposed secondary infection. Herpes, Tuberculosis,

Neoplasm are rare causes but do exist. Syphilitic

Infection - be it the Primary or Secondary Stage (condyloma) of the disease is very often misleading.

Spirochaetes of a coarser variety than Pallida occur as Saprophytes in the Genital region e.g. S. Refringens, T. Minutum; T. Calligyrum should not be confused with Sp. Pallida but clinically one may be misled by a scanty watery discharge, which may be due to an Intraurethral chancre or perhaps it may be situated in the Vagina or Cervix.

Therefore the importance of Clinical as well as Bacteriological Examination is essential.

Soft Sore can also occur but again Clinical appearance and identification of Ducrey's Bacillus should cause no difficulty. In the series of cases under review Gonococci were isolated in 82% of cases at the first examination. Repeated examinations raised the figure to 97% i.e. from either urethra, Vagina or Rectum or from all.

In the remaining 3% other factors aided in a provisional diagnosis e.g. Gonococcal Complement Fixation Test, history, clinical Examination etc. Worms (of the Oxyuris type) accounted for two cases. One child had associated Gonococcal Infection and acquired Syphilis - the primary lesion being situated in the Labial region.

To recapitulate a few facts to be considered in the Differential Diagnosis:-

1. Note the History carefully - probable explanation of the condition - previous illness etc.
2. Careful clinical examination of the parts likely to be affected.
3. Repeated Bacteriological Examination of the discharge.
4. Examine the Rectum in every case for Threadworms.
5. General Systemic Examination if the previous four criteria fail e.g. Syphilis, Tuberculosis etc.

Below, we have attempted to tabulate the commoner aetiological factors:-

#### BACTERIOLOGICAL

<u>More Important Organisms.</u>	<u>Lesser Important Organisms</u>
1. Meningococcus,	1. Staphylococcus Streptococcus Diphtheroid Bacilli. etc. (usually secondary infection).
2. Micrococcus Catarrhalis,	2. Furunculosis (Staph. Aureus).
3. B. Diphtheriae,	3. B. Tuberculosis,

More Important Organisms.      Lesser Important Organisms

4. Streptococcus of  
Scarlet Fever.
5. Pneumococcus.
6. Sp. Pallida,
7. B. Ducrey.

Others

1. Trauma,
2. Worms ,
3. Tumor,
4. Dirt and Debility,
5. Herpes ,
6. Diabetes Mellitus etc.

P R O G N O S I S

We shall consider from two aspects

(a) immediate and (b) ultimate.

IMMEDIATE

58

a. Dooley says that seldom does one see complications occurring during the acute stage of the disease and relatively uncommon in the latter stages. But this advantage is outweighed by the intractability of the disease - a point already emphasised repeatedly. Clinically the child may appear cured but one must aim at radical cure. This requires time and observation and this is the stage so difficult for the relatives to understand. For the time being, one can assure them that the disease has every chance of being cleared up. The advent of puberty in itself would seem to be the final blow to the Gonococcus in fully 95% of cases. (Personal observations revealed no cases where a coexistence of menstruation and Gonococci were found). But to ensure a healthy normal "puberty" the structures involved must be maintained at a healthy standard. Hence the reason for attempting to exterminate the disease rather than wait until the puberty age before which irreparable damage may have been done.

And furthermore imperfectly treated cases lead to two great "curses" (a) Carriers (b) Relapse. From all that has already been said, "Carriers" are self-explanatory. (b) Relapse - The percentage of

Relapse in our clinic was 8.6% - really an eminently satisfactory figure considering the nature of the disease plus the fact that many of this group attended as out-patients and apart from being free from restrictions which otherwise would be imposed on them in Hospital, certain of them failed to attend for treatment or examination at the appointed time.

Even so, with all our treatment, care, and diligence, both on the part of the patient and medical staff - relapse did and will occur in a small percentage, but as already said the prognosis is favourable.

I agree with Kimball that the prognosis is better in the younger children especially under one year of age. All our more obstinate cases, also those of relapse occurred after that age.

#### ULTIMATE

About this we can say very little. Before passing a verdict, the case or cases would have to be "followed up" even during her married life - a very important phase of the woman's life according to many authorities, who are definitely of the opinion that it does cause anatomical damage with resulting impairment of development. For example, Martin says, imperfect development of the Genitalia and chronic invalidism of later years is due to Gonococcal Vulvo-Vaginitis in early life. Also Currier holds, that an underdeveloped uterus associated with which may be sterility, dysmenorrhoea etc. may likewise be due to this disease. Vogt attributes extra uterine pregnancy to it, in a large percentage of cases.

On the other hand however, Matthisohn,<sup>59</sup>  
 Wolffenstein,<sup>60</sup> Pontopiddan,<sup>61</sup> Von Buschke and Gumpert<sup>62</sup>  
 maintain that the ultimate prognosis is quite good.

Parker Dooley gives the following figures:-

32 cases menstruated at normal age and intervals.

8 had menstrual cramps and backaches.

5 had leucocchoea.

No cases of incapacitating dysmenorrhoea.

17 were married - 10 were mothers - 2 were pregnant.

Koplik<sup>63</sup> quotes numerous cases illustrating that such women frequently have children.

Kjellberg Romanus<sup>64</sup> gives the following results.

Total number 49 cases.

27 were normal healthy women and the other 22 had various forms of dysmenorrhoea.

Taking it on the whole then, the prognosis could be much worse. In itself, the disease is rarely fatal - It is one which is overcome ultimately. That part of the body liable to suffer as an aftermath is the Reproductive system, and one gathers that the general concensus of opinion favours the more optimistic side of the question.



G O N O C O C C A L   C O M P L E M E N T   F I X A T -  
I O N   T E S T : -   I T S   V A L U E   I N

P R O G N O S I S

As already mentioned our experience with this test from the Diagnostic point of view is limited. Consequently one cannot discuss its Prognostic value, from personal experience, very much. Only in about 7% of our cases was it employed and briefly putting it, it was of little use. The question of antigen formed by the body tissues has been discussed at some length already. During treatment, in 78% of cases, one employed Vaccine Therapy to further stimulate antibody formation. This probably explains to a large extent why conflicting results were obtained. For example we obtained the following results:-

(a) Patients clinically and bacteriologically cured showed a positive Gonococcal Complement Fixation Test, 2 and often 3 months afterwards.

(b) Patients still showing Gonococci in the "smears" revealed a negative Gonococcal Complement Fixation Test following on a period during which it was weak positive. In 80% of this group however no Vaccine Therapy was employed which perhaps had something to do with the Serological results.

The few observations made on this test with regard to Prognosis we shall now endeavour to summarise. Its value in Gonococcal Vulvo-Vaginitis as compared with adult Gonococcal Infection is somewhat limited, since it is believed to reveal latent foci and complications of Gonococcal origin early in the disease. Re. the latter, one had little experience, but pertaining to the former i.e. latent foci, it served a useful purpose in two or three cases in particular where Gonococci had never actually been seen on microscopical examination.. It did not act as a useful aid in detecting complication since clinical observations were sufficient.

The interpretation of the degree of positivity with regard to the Prognosis must be done intelligently e.g. a case showing a ~~++~~ positive test need not imply infection present in a fully treated case and especially where Vaccines have been employed. It is the reduction in the degree of positivity which matters i.e. a case previously showing a ~~++~~ now showing a + implies a definite improvement in the patient's condition. Naturally, a severe infection demands a longer time for the Serological result to become negative. Antibodies are present usually in the blood for 5 - 6 weeks after the infection according to Shupe.

<sup>57</sup>  
Magner maintains that Vaccine Therapy does not prolong the duration of positivity in the absence of Infection. One cannot agree with this from the small series of cases under observation.

Repetition of a negative Gonococcal Complement Fixation Test does not imply freedom from infection. One must ensure complete absence from infection by repeating the test about four weeks later. Thomson holds that a "Cured" case should show a fall in positivity at the rate of one plus per month so that by the 3 - 6 months the patient should be serologically negative. With this one agrees; most of the cases in question in this series showed a decrease in positivity at the rate of + per month on an average. All the cases save one, were "negative" by the 17th.

week and this exception took 5 months.

So that from the prognostic point of view this test was more useful, than as a diagnostic procedure. One might conclude by suggesting that "taking" the Gonococcal Complement Fixation Test might be a useful guide to the reaction to treatment of such a protracted disease as Gonococcal Vulvo-Vaginitis, at monthly intervals.

PROPHYLAXIS

This to our way of thinking is one of the most important "links in the chain". If the importance of prophylaxis could be sufficiently impressed on the minds of the Medical Profession as well as the lay people, then less would be seen of this disease.

The Education of the Public is a big factor. The failure of medical men to (1) impress on the infected adult the importance of the disease from the infection point of view is probably the crux of the whole matter. As a result, numerous cases of Gonococcal Vulvo-Vaginitis arise from girls sleeping with infected parents, using the same towels, clothes etc. (2) eliminate the disease from the adult i.e. uncertain and varied criteria for the test of "cure" in infected adults. Also the failure to recognise the so called "Whites" in the adult female as being Symbolical of a chronic Gonococcal Infection in many such cases.

More careful and energetic measures when admitting children to Institutions ~~were~~ other children live. "Carriers" of Gonococcal Vulvo-Vaginitis as we have seen may show little evidence subjectively or objectively, hence the suggestion put forward by certain authorities that all children admitted to Children's wards in Hospital should have Vaginal Smears examined, is a good one. The suggestion put forward by Watson, Taussig and others that Gonococcal Vulvo-Vaginitis

should be made a Notifiable Disease seems sensible, but as Lees<sup>5</sup> points out the necessary facilities and accommodation for treatment would require to be more generalised and improved than they are at present. All fresh cases should be Hospitalised - the source of infection determined if possible and the other young girls in the household examined as a precaution.

And a final measure to reduce the frequency of Gonococcal Infection is put forward by Taussig. He recommends instillation of 2% Silver Nitrate into the Vestibular and Vaginal parts of all new born children.

When the case has actually developed one would suggest the following procedure.

(a) Immediate isolation of the case. Treat it as an infectious disease. Seldom are there the facilities to treat the little patient at home.

(b) The determining, if possible, the source of infection, be it another child, adult, inanimate objects e.g. Towels, lavatory seats etc.

(c) Careful Observation of every young female in that house, institution etc. likely to come in contact with the child. If in a private house investigate every member of the household, the child's associates at school and elsewhere etc.

(d) Skilled nursing is an essential prophylactic measure. This can only be appreciated by one who is acquainted with the infectiousness of the disease,

with the risks of self infection which the young female runs. Consequently, steps must be taken to minimise those risks, e.g. complete disinfection, after use, of the lavatory seat; likewise the eliminating of the possible danger of fingers, infected from the genitalia, transmitting the disease to the eyes etc.



T R E A T M E N T

Although this disease is considered by some authors a self limiting one it demands still, care and above all patience in treating the condition. Like most diseases treatment may be subdivided into General and Local.

ACUTE STAGE

General The little patient should be confined to bed as movement exacerbates the severity of the condition. The Bowels should be carefully attended to - an initial purge followed by a daily saline draught if need be. Likewise the diet should be mainly fluid in the initial phase and if the disease be less acute a low Protein diet may be given (Protein being reduced on account of its Thermogenetic properties). Large quantities of fluid should be given to promote diuresis. Attention to the clothing is equally important. The child lying in bed requires little clothing but special attention to the garment next to the ano-Genital region is essential. Closed rubber pants are by far the best in the young children, and in the case of older ones cotton knickers which should be changed twice daily. The whole object ofcourse is the immediate disinfection of the garment once removed and of such a material which is economical and can stand vigorous antiseptic treatment.

Gonococcal Vulvo-Vaginitis is extremely contagious among young girls, therefore, no attempts



should ever be made to treat the patient at home, i.e. Hospitalisation is essential. Each and every case should be treated as an "isolated" one - the nurse taking elaborate precautions against "cross infection" or in any way transmitting the disease to any other young girl. Hence her own personal hygiene besides that of the patient's must be considered. This especially applies to her fingers which should be treated with rigid precautions after attending such a case. Similarly, in a Children's Ward Gonococcal Vulvo-Vaginitis children should have their own utensils e.g. rectal thermometer, sponges, baths, towels etc and no one else's. The nurse too, should guard against one of the most dangerous vectors - the lavatory seat - the U shaped seat being the ideal one and, when used by an infected patient, should be covered with a paper cover, which should be immediately destroyed after use and <sup>the</sup> seat suitably disinfected. The habits of the little patient should be carefully watched - itchiness is liable to cause the child to scratch the parts with possible dangerous sequelae (a) immediate - that of transmitting the infection to other parts of the body and especially the eye, (b) increasing the severity of the infection locally, (c) Masturbation - which is difficult to eradicate and often maintains the chronicity of the disease.

With regard to more specific general treatment. An alkaline mixture should be given orally thrice daily. Such a mixture might contain

Potassium Citrate, Potassium Bicarbonate, and Infusion Buchu with Tinct. Belladonnae (Children usually tolerate Belladonna very well) if need be, to counteract vesical spasm. Hot Hip Baths are one of the prominent features in our treatment. A small amount of antiseptic plus Sodium Bicarbonate is added to the water. The latter aids in cleaning away mucous and in addition renders the bath more soothing. Apart from the soothing influence those baths have additional advantages (a) mechanical action - washing away dirt, pus etc. around the ano-genital region. (b) produces a mild hyperaemia beneficial to the inflamed parts (c) a mild antiseptic action, Sod. Bicarbonate relieves any itch which is often present. Just a little word of warning, here regarding the transferring of the child to the bath - the nurse should lift the child taking care that neither her nor the child's hands should come in contact with the infected parts. Moreover, care should be exerted in placing the child in the bath the temperature of which should also be regulated. Only too often does one see a careless nurse plunge a child into a bath the temperature of which is much too hot. The effects on the child are obvious - apart from the psychical effect of the sudden shock which may entail great difficulty in persuading an older child to have another bath, the inhibitory effect on a rheumatic heart is obvious. The nurse should "test" the temperature of the water with her bare elbow, if a thermometer is not available - too hot or too cold a

temperature is equally dangerous.

These points may seem trivial but to my mind are important and as said already, are extremely important both from the therapeutic and psychological point of view, to the patient. Brown has rightly emphasised that too many hip baths are dangerous mainly for two reasons:-

- (a) rendering the affected parts sodden and thereby encouraging the disease.
- (b) liable to cause urine incontinence.

#### Local Treatment

From personal experience we have no hesitation in saying that IRRIGATION undoubtedly is the important factor here. Other local measures are regarded as accessory factors.

The child is transferred from the Hip Bath to the table and placed in the lithotomy position in a good light. The Genitalia are cleaned with Eusol swabs, mopping away any discharge if there should be any present. Open the Vulva gently with thumb and forefinger of the left hand - take a Vaginal "Smear" with a Platinum loop and then insert the nozzle of the irrigating outfit. One never had occasion to employ General Anaesthesia with our cases at the initial irrigation.

Herewith I append the apparatus used in the Edinburgh V.D. Clinic.

- (a) A Glass Douche Can (capacity 4 pints)

(b) Rubber Tubing 4-5 feet long

(c) Vulcanite Tap attached to the distal end of the rubber tubing which in turn is connected to the apical (lower) end of Douche.

(d) Narrow tubing - a few inches in length leading from the other end of the Vulcanite tap to a

(e) Kidd's Glass Catheter - the distal end of which is perforated with numerous small holes the purpose of which is to obtain maximum access to the crypts and thus flush out the Vagina thoroughly

(f) "Platinum" loops.

(g) Eusol and Swabs.

(h) Playfair's Probes ("dressed")

(i) Glass Speculae

(j) Insufflator (preferably of the De Vilbiss type).

(k) and Pail.

### Technique

About one pint of antiseptic lotion (which will be discussed in detail later) is put into the douche can; insert Kidd's catheter about one inch distance into the Vagina; turn the stopcock and allow the antiseptic to run in slowly (regulating by the tap) - the head of flow never more than two feet above the Pelvis; the backflow from the Vagina is allowed to run into a pail at the operator's feet; Having irrigated the Vagina thoroughly, turn off the flow, withdraw the "catheter" (thus allow the Vagina to drain itself) - detach the Catheter from the rubber

tubing and replace it by a smaller sized one. This is inserted as far as half an inch into the urethra and the irrigation continued.

Having used the pint (approximately) of irrigation and cleansed both the Vagina and urethra thoroughly withdraw the "catheter" from the urethra. Insert a glass speculum (of suitable size) which has been dipped in olive oil, into the Vagina. in the Postero - Inferior direction, swab out the Vagina gently with "dressed" probes till the parts are dry, then insufflate through the Speculum a powder such as "Dermatol" (which proves to be very satisfactory), pass a dressed probe into the Vagina, withdraw the Speculum over the probe and then withdraw the probe itself - thus leaving the interior absolutely dry. Finally the external genitalia are insufflated with "Dermatol" powder the composition of which is as follows.

Zinc Oxide	One Part
Light Magnesium Carbonate	Two Parts
Bismuth Subgallate	Two Parts
Powdered Starch	Three Parts

Following which treatment, the child is put to bed. In younger children one finds a vulvar pad very useful since it absorbs all vaginal discharge or secretion and thus prevents irritation of the thighs; further it is soothing and in addition may have a mild antiseptic effect ( all depending on the type of pad used). Ordinary gauze was found to be quite efficient.



Intertrigo in the Inguinal region due to discharge is often troublesome and we found Lassar's Paste applied b.i.d. very efficient. As the acute phase passed off one accordingly modifies the treatment.

General By this time the Diet is a nourishing one containing plenty of Vitamins and Bowel Roughage. Tonics containing Iron, Strychnine etc. or Cod Liver Oil and Malt and other Vitamin containing preparations may be given where need be. And above all, plenty of fresh air and sunshine.

The Hip Baths are gradually dispensed with.

Locally : - irrigation is still given twice daily - the antiseptic being changed at approximately 10 - 14 days intervals.

Pessaries were used at this stage as follows

A. Vaginal in 36% of cases

B. Urethral in 28% of cases

Among the numerous varieties one found the following the more efficient.

Mercurochrome	$\frac{1}{4}\%$
Lunosol	10%
Picric Acid	$\frac{1}{2}\%$
Albargin	$\frac{1}{4}\%$
Picric Acid and Glycerine	1%
Spumen with Icthyol	15%
" " Silver	2%
" " Acid Salicylic	12.5%

In addition Lactic Acid and Citragan Pessaries were also employed. Our results like those of Watson's from pessary treatment were extremely disappointing. It does not matter which type one selected the result was always the same - no shortening of the positive phase of the Illness.

Gradual improvement leads to reduction in the frequency of treatment and the strength of the antiseptic. A Hip Bath for purposes of cleanliness is all that is given during this period. The child should be allowed to run about. Often in the Sub-acute and Chronic Stage, in the cases under review cervical involvement has occurred. Admittedly it was never very severe but well nigh intractable. Mercurochrome 20%, Silver Nitrate 5 - 10%, and 1% Picric in Glycerine, were all tried. The last was found to be the more satisfactory, but truth to tell there was not much in it.

The amount of treatment at this stage is controlled by Clinical and Bacteriological results. Complete negativity of both is followed by suspension of treatment during which a close watch is kept clinically and bacteriologically. Three weekly consecutive negative smears from urethra, Vulva, Vagina, warrant a test for cure in the near future.



C O N C L U S I O N S

Treatment varies in different hands, from simple hygienic measures to the most painstaking local applications, but it is for the most part empirical and frequently irrational. Methods innumerable have been tried out in this disease, all having the same result. The more one sees of the disease, the more one is convinced that, as we stand at present, no one can be dogmatic in laying down definite lines of treatment. Furthermore, the multiplicity of methods support this view.

Undoubtedly our method, just outlined is subject to many flaws e.g. why do we take such great pains to keep the vagina dry while as we are fully aware, the urethra also a potent focus of infection is simply irrigated and left at that. This argument has been put up against the practice of irrigation. Those who are antagonistic to this method of treatment also maintain that changes in the Vaginal secretion ensue; that the Vaginal Wall ultimately resembles that of the Senile Vaginitis thereby reducing local resistance and keeping up the infection. To one's mind the answer to that question is, asking the prime aims of local treatment. Drainage is essential to eliminate the infection. This we have seen follows on irrigation (the temperature of which is about that of body temperature) which also promotes a mild hyperaemia i.e. stimulating local

resistance. As regards the urethra the possibility of keeping it dry is obviously well nigh impossible. The child is drinking copiously, mild diuretics are being given, and consequently frequency of micturation due also to local irritation makes this quite impossible.

The important fact that dryness is lethal to Gonococci is foremost in our treatment - the careful dry swabbing and powder insufflation being self explanatory on that point. Also while it demands care, much time, and patience, the methods employed are relatively simple and few in number.

This does not imply however, that other methods employed elsewhere have not been given a trial. The question of Pessaries has been alluded to. Packing the Vagina with clean gauze, or with gauze soaked in Glycerine plus one or other of the antiseptics and left in 24 hours, has been tried with similar results - In two cases in particular we had relapses, where the discharge was increased, a return of Gonococci in the Smears, and increased local irritation and discomfort to the patients. Painting the affected parts with mercurochrome in varying strengths - in some cases as strong as 20% - and with  $\frac{1}{2}\%$  Picric Acid in Glycerine was also tried, but results did not warrant a further trial.

Measures employed by other authorities have been proved equally unsuccessful e. g.

(a) Local application of ointments containing the various commonly used antiseptics.

<sup>65</sup>  
 (b) Lode used Thermal Baths but found them not only unsuccessful but also dangerous - so much so that he warned others against their being used. Schulz<sup>66</sup> however, found them beneficial.

(c) The same author employed deep hot baths as recommended by Weiss. The child was given as many as 15 daily for about 10 - 15 minutes every second day, the temperature being gradually raised from 38 to 44 degrees Centigrade. He reported a transient improvement but other effects notably, headache, abdominal cramps, delirium and even syncope, forced him to discontinue this form of Therapy.

(d) Reith fraser recommends hot Rectal Douches morning and evening as a local measure quite independent of : -

#### PROCTITIS

The few cases which one had to treat were irrigated after a manner already described. They showed a slow but steady response to treatment - no relapses. Irrigation was the sole line of local treatment.

ANTISEPTIC THERAPY

Is it essential? Such may have been a point open to dispute about Wagner's time when he experimented with irrigating VulvoVaginitis cases with sterile water at a temperature of about 45° Centigrade. Apart from gross discomfort to the child, his results soon convinced him that the method was a failure. His incidence of relapses, protracted duration of cases at various stages of the disease, compared unfavourably with those who were experimenting along the same lines but using antiseptics in place of sterile water.

Various methods and various kinds of antiseptics have, and are being tried at present, of which one will mention a few:- Buckley-Sharp - previously employing Potassium Permanganate irrigation followed by an acriflavine Pessary, and supplemented with bi-weekly swabbing of the parts with Silver Nitrate, - switched over to Douching followed by packing with ribbon gauze soaked in one of the following:

a.	Glycerine	+	Flavine	1%
b.	"	+	Protargol	10%
c.	"	+	Auramine	1/30
d.	"	+	Speton $\frac{1}{2}$ tablet	to one drachm.

He found, packing of the Vagina after

irrigation reduced the duration of the disease by 3 weeks on an average.

Like many other authors, he bases the efficiency of the methods on an average period over a number of cases before the patient was cured. His figures were as follows. (a) Former method of treatment 5.74 months - longest case taking  $13\frac{1}{2}$  months; (b) latter method 4.9 months and 12 months respectively. Brown at Guy's Hospital, regards Potassium Permanganate 1/10,000, Glauramine, Dibromine, as best for irrigations. Local applications were also employed chief of which were Spumen (with or without Propargol) 10% in Glycerine, Mercurochrome 10%, Emulsion of Sulphur or Flavine 2%. She found that the average duration was 18 weeks - Range 4.39 weeks. Kurzwell and Saxl found acute cases lasted 6 - 8 months before cure: Other cases 10 - 12 months before cure. Maggiore<sup>67</sup> followed irrigation with Potassium Permanganate 1/20,000 followed by careful drying and putting a pad over the labia to keep the parts separated. Duration 1 - 3 weeks. Gellhorn employed 1% Silver Nitrate in a basis comprising equal parts of lanoline and white petroleum, and claims this to be a very satisfactory form of treatment.

Hamilton employed at various times physiological Salt Solution, Potassium Permanganate 1/4000, Boric Acid 3%, Formalin 1/1000. Simmins<sup>68</sup> finds 1/5000 Flavine very efficient. Harrison<sup>69</sup> believes



in Chloramine T 1/5000 followed by swabbing the parts with 25% Mercurochrome 220,<sup>70</sup> weekly. Bland and Brunet advocate the application of Lugol's Iodine Solution. Patschke<sup>71</sup> adds adrenalin 1/1000 in a strength of 1/20 to a .5% solution of Albargin to intensify the action of the Silver. Norris advocated Potassium Permanganate followed by swabbing the parts with 25% Argyrol, drying the parts thoroughly with an atomiser/for half an hour at the end of which time he paints the affected areas with 2% Silver Nitrate every second day, increasing the strength of the Silver Nitrate as tolerated by the patient. Abraham<sup>72</sup> advocates douching, followed by tamponage containing a paste of Bulgarian Sour Milk and castor sugar (half the bulk of milk). Titus and Notes<sup>73</sup>-employing 1% Cresol plus Sodium Bicarbonate, found the "duration" period, on the average, to be 10 months with a 6% "recurrence" incidence.

From the foregoing facts one observes that irrigation as a means of applying the antiseptic to the involved area, was not the only method. Pessaries, Tampons, Painting the antiseptic directly on the affected parts, were also employed. The relative merits of these methods were as inconclusive as the efficiency of the various kinds of antiseptics. The information on the whole problem is anything but helpful. What one author finds useful another condemns e.g. Silver Preparations are held in high esteem by Schaffer<sup>74</sup> while Finger and Ghon<sup>75</sup> condemn them. Tampons, according to Hamilton, are a failure while Buckley-Sharp

finds them the contrary. Brown in her series of cases finds Pessaries of eminent value while again this is refuted by others.

Thus we have a wholesale disagreement regarding the choosing of routine treatment suitable for the average case. This applies to a lesser degree regarding the method of bringing the antiseptic in touch with the Gonococci by means of irrigation but, even here the type of antiseptic is also subject to much dispute. Certain of those authorities chose their antiseptic with regard to its efficiency and quality of an antiseptic, regardless of the effect which it may have on the tissues. Others again while observing the importance of the efficiency of antiseptic, appreciated more the need for bringing it into intimate contact for a considerable period with the Gonococcus e.g. packing the Vagina. Equally important of course was the keeping of the parts dry. Many failed apparently to appreciate the fact that dryness is lethal to the Gonococci. Further, one does not observe much changing of the antiseptics during treatment, i.e. what one proposes to call "monotherapy" with regard to Antiseptics. Another important point - Were the tests of cure adopted by each authority more or less the same? If not, and it does not seem likely, how can the efficiency of any one line of treatment advocated by its vaunter be regarded as such? This question of the tests for cure probably explains, as much as the efficiency of



the method of treatment, why varying figures were obtained regarding the "duration of treatment".e.g.

1.Buckley-Sharp	(a) 5.74 months (b) 4.9 "	Old Method. New Method.
2.Brown	4 $\frac{1}{2}$ "	
3.Kurzwell & Saxl	(a) 6.8 " (b) 10 -12"	Acute cases. Less acute & chronic cases.
4.Maggiore	$\frac{3}{4}$ "	
5.Titus & Notes	10 "	
6.Kidd & Simpson	4 "	
7.Reith Fraser	3.2 "	
8.Stein <sup>76</sup>	2.4 "	
9.Williams	5.0 "	

Obviously from the above, antiseptics alone cannot explain away why, certain cases cleared up before others. Admittedly they are of great value, but in employing an antiseptic one must not only consider its effect on the "seed" but also on the "soil".

To sum up the qualities required of an ideal antiseptic in the treatment of Gonococcal Infection would epitomise the difficulties with which we have to contend and also the ideals aimed at in this form of therapy.

The Ideal Antiseptic should possess the following.

1. It must be a powerful gonococcide in weak solutions (Seed).
2. It must be well tolerated locally and non toxic (Soil).

- 3 Should not coagulate albumen (Soil).
- 4 Water soluble, stable with regard to light (Intrinsic Properties).
- 5 Power of penetrating the tissues and sustained bactericidal action. (Seed and Soil).
- 6 Should not be rendered inert by urine or the tissues ( e.g.Salts such as Chlorides - Intrinsic Properties)
- 7 Should be Hygroscopic rather than astringent when used in relatively concentrated form (Intrinsic Properties).
- 8 Should be inexpensive and accessible to the community (Intrinsic Properties).

(The various terms in parenthesis after each "property" of antiseptic indicated in which direction that "property" exerts its advantage - Soil ofcourse, means the tissues; Seed - the Gonococcus).

Therefore, we see that the lethal powers possessed by an antiseptic, matter relatively little in this line of treatment. As it so happens, Gonococci are extremely susceptible to the weakest of antiseptics, but unfortunately while this is possible to prove experimentally "in vitro" a more difficult problem presents itself "in vivo", that of gaining access to the organism. This condition may arise naturally in the course of disease - the Gonococci penetrate into crypts, Glands, Submucosal regions etc, and therefore, are in some cases well nigh inaccessible to action of antiseptics. Such a substance comparable to the penetrating powers of Tryparsamide in Neurosyphilis would be of decided advantage here. Irrigation itself, mechanically aids penetration but to a relative minor degree.

Again however, inaccessibility may be further increased by the antiseptic itself, (In passing, one would mention such substances as certain silver salts) due to its astringent action. Such substances by virtue of this defect defeat their purpose, as will be illustrated later.

Furthermore, the action of certain antiseptics is almost lost in some cases, where chemical reaction between the antiseptic and the tissues (especially the chlorides) ensues - the positive Ion of the antiseptic combining with the negative Ion of the salts or vice versa. Apart from this, the "product" of chemical reaction is thus practically inactivated and therefore, the antiseptic qualities have disappeared.

Again Biochemical reaction must also be considered. Schlagenhauser<sup>75</sup> found that Mercury Perchloride in saline 1/5000, Silver Nitrate 1/1000, coagulated the albumen in the tissues and prevented penetration of the antiseptic to deeper seated sites of Gonococcal infection.

We have dealt with the active phase of the antiseptic, let us now consider the "passive" phase: - namely, the effects on the tissues if any of the antiseptic in performing, or attempting to perform its duty?

Gonococci like every other organism cannot settle in the tissues without the latter

assuming defensive measures. Such measures express themselves in the form of inflammation where naturally the tissues are considerably devitalised.

Superimposed on the bacterial, we may have a chemical irritant with which the defences have to contend successfully or otherwise. If the latter, then the vicious circle is set up the effect of which at first local may become general. Such may happen when an antiseptic unsuitable regarding strength or chemical composition is employed.

It is safe to say, that there is no substance credited with the slightest antiseptic or astringent power which has not been used for local application to the urethra. The chief survivors may be divided into:-

1. Preparation of Silver.
2. Potassium Permanganate.
3. Mercurial Solutions.
4. Halogen Series Chloramine T, Dakin's Solution, Proflavine, Acriflavine etc.
5. Astringent Solutions of the Sulphates of Iron Zinc and Copper.
6. Dyes - Gentian Violet, Methylene, Blue etc. and other coal tar derivatives.
7. Bile Salts.
8. Local Antiseptics - Holocain etc.

Recently numerous others, which do not fall into any of the above groups, have been tried out. A few of these are discussed below. One does not limit the various types of antiseptics to various stages of the disease so rigidly, as say in adult male Gonococcal

Infection but even then judgement must be used e.g. an astringent lotion is obviously to be used later in the disease to promote healing rather than in the earlier and acute inflammatory phase.

The numbers of antiseptics employed in the Edinburgh V.D. Centre are legion but herewith we append a few of the more important.

Potassium Permanganate	Silver Nitrate
Iodine	Formalin
Citragen	Hydrogen Peroxide
Picric Acid	Mercurochrome 220
Chloramine T.	Lactic Acid
Flavine	Sodium Bicarbonate
Albargin	Hydrarg Perchlor
Arvitin	Argurol
Lunsol	

The more important of the above list will now be discussed briefly - referring to our experience as compared with that of others.

#### Picric Acid

We agree with Turner<sup>77</sup> (who obtained excellent results from Picric Acid in treating adult females), that Picric is one of the most suitable antiseptics in the treatment of Gonococcal Vulvo-Vaginitis, especially so in the earlier stages of the disease rather than the more chronic phase. Moreover one can use it in strengths of 1/400 in glycerine.

#### Potassium Permanganate

Another extremely useful antiseptic in our experience. One cannot agree with Swartz<sup>78</sup> and Davies that it is too weak a gonococcal substance to have any effect on the organism "in vivo". Maheu's<sup>79</sup> observation regarding the bactericidal effect of this antiseptic on the Gonococcus is more in keeping with our findings.

At the same time, records do not warrant its superiority over Picric Acid. The low incidence of relapses and the maintenance of improvement was not observed in these cases where Potassium Permanganate predominated as compared with Picric Acid. Iodine in Oil, was recently introduced and although it has not had time yet to justify all that has been said about it, its efficiency is equal to that of Mercurochrome 220, which Williams regards as a highly useful antiseptic. He found the average duration before a smear



was negative was 3 - 4 weeks as compared with Argyrol where the corresponding period was 7.5 weeks. We found that for similar periods, Mercurochrome produced a 75% difference in the degree of positivity as compared with Silver Nitrate (25%). Other antiseptics of the Halogen group - Flavine, Proflavine, Acriflavine while satisfactory, did not justify all that has been said for them by Watson, Davis, Hamell and others. Harrison<sup>30</sup> finds Potassium Permanganate every bit as satisfactory as Acriflavine. Mercury Salts especially the Oxycyanide, is quite a useful antiseptic, but has one disadvantage, in that it tends to prolong the period during which Pus cells are present.

Silver Salts - do not occupy the place formerly held, owing to certain drawbacks quite apart from their antiseptic value. Silver, by reason of it being a heavy metal coagulates albumen in the tissue i.e. impairs access to the Gonococcus and as a result encourages the organism to bury deeper in the tissues. Schaffer has a very high opinion of Silver Salts since they remained longer in the tissues. Perhaps Schaffer did not realise that the probable reason for the prolonged "stay" of Silver in the tissues is because it has caused a reaction in the tissues resulting in the coagulation of Albumen. Moreover, he points out that a further advantage of Silver Salts is that they can be used in high concentration. Is this necessary to kill the Gonococcus? Apart from that is it desirable - the effect of strong antiseptics on the tissues?.

Statistics of the cases under review showed that the antiseptics employed, occurred as follows.

<u>Antiseptic</u>		<u>Average Strength</u>	<u>Percentage of Cases,</u>
1	Picric Acid	1/400	90
2	Potassium Permanganate	1/6000	85
3	Silver Nitrate	1/20000	45
4	Mercurochrome	1/1000	43
5	Arvitin	1%	30
6	Chloramine T.	1/5000	25
7	Citragan	33 1/3%	22
8	Albargin	1/6000	10
9	Flavine	1/400	7
10	Lactic Acid	1/500	5
11	Hydrogen Peroxide		5
12	Iodine	1/40	4 recently introduced
13	Formalin		2
14	Hydrarg Perchlor	1/5000	2

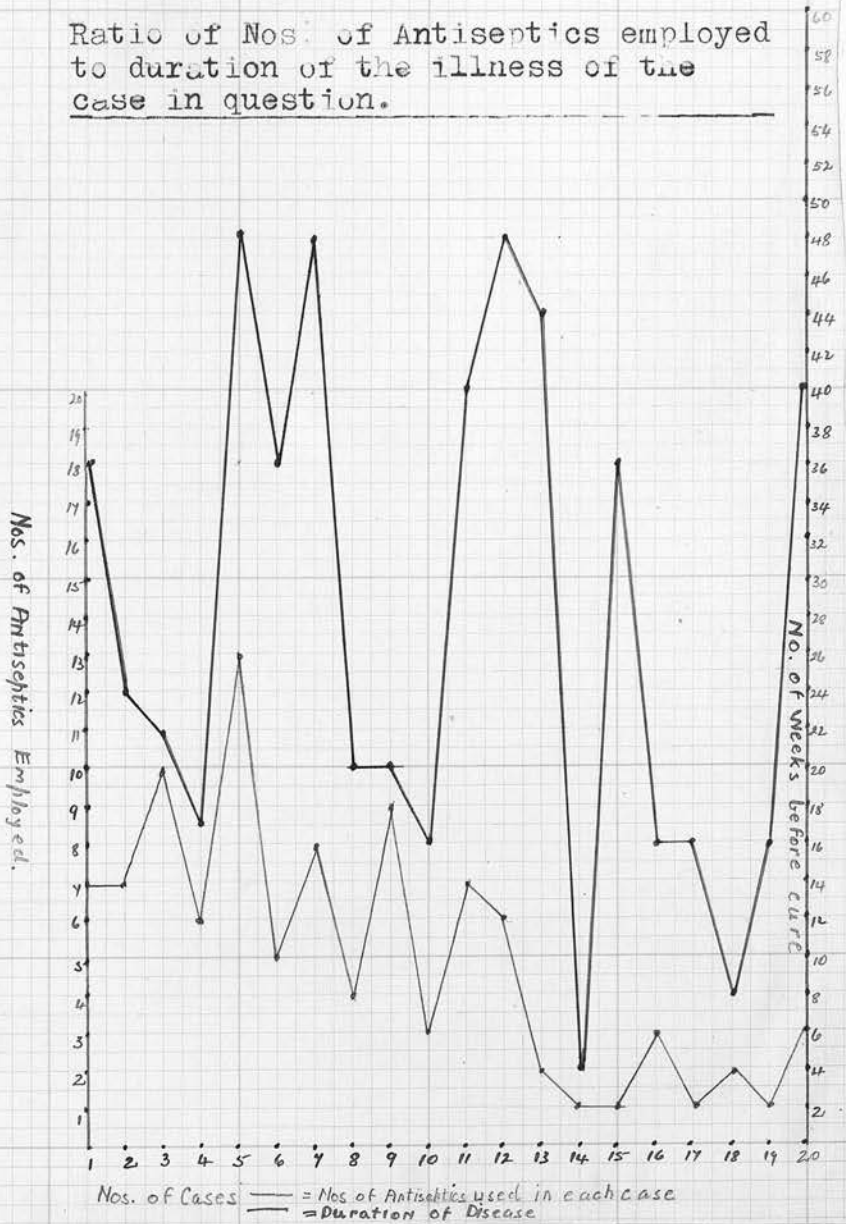
Such a table must not be taken at its face value. A few of the antiseptics which have been recently introduced will or will not get a protracted trial, all depending on the results obtained. A few of the antiseptics at the top of the list have been used more than once in some cases. This would seem to warrant their efficiency in dealing with this problem satisfactorily. But do they?

Does the secret of antiseptic therapy lie in the practice of changing the antiseptic periodically? A very few of the cases have been tried on "monotherapy" but the results were far from satisfactory. Again, most cases were tried on numerous antiseptics during their treatment, with the hope that the duration of the disease might be abbreviated. Selecting twenty cases at random one obtained the following results.



CHART No. 1VCHART No. 1Vshowing

Ratio of Nos. of Antiseptics employed  
to duration of the illness of the  
case in question.



Probably the above number of cases is too limited to draw definite conclusions, but it is quite apparent from the chart that "ringing the changes" does not imply shortening the course of the disease. One was rather impressed with this observation and decided to investigate every case under review in detail and the gross result was in keeping with the chart. To be precise 22% of the

total number seemed to benefit by changing the antiseptic frequently while the remaining 78% were affected in the opposite manner.

So that from personal observation the ringing of the changes does not seem to be of prime importance. But this does not imply the variety of antiseptics should be limited to a very few. Quite the contrary, and at this point one would like to discuss the choosing of the antiseptic with regard to the stage of the disease. Silver Nitrate was used in approximately 50% of cases, and closer investigation showed, at that time of the disease, corresponding to the subacute phase more or less. Now Silver Nitrate, as we have repeatedly emphasised drives the Gonococcus into tissues and forms a barrier which is protective to that organism. From our personal observations this was only too true.

To illustrate the point:-

Below is a chart typical of the "Silver Nitrate case" where it has been employed, about the Subacute Phase.

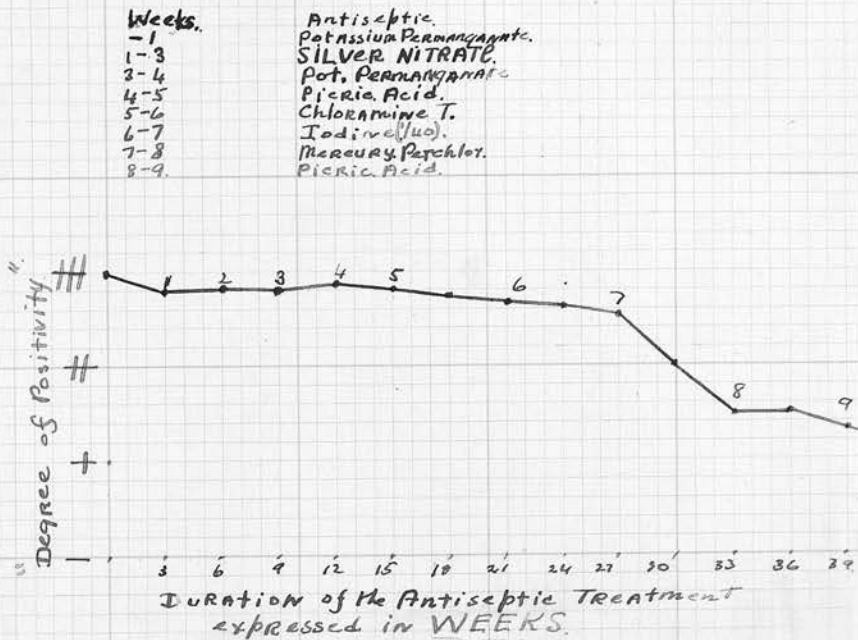
The Horizontal line indicates the number of days on each antiseptic and the Vertical - the degree of Positivity. By this we mean the bacteriological examination of the film - the presence of Gonococci being represented by †, ††, ††† varying as to the numbers of Gonococci per microscopic field. Pus cells also are considered as an index to antiseptic efficiency in the absence of Gonococci which are the

prime guide. (In passing, one should say that the Bacteriological aspect is regarded as more accurate than the clinical, since there may be nil or little to note subjectively or objectively) and yet the patient harbours Gonococci in fairly large numbers.

### CHART No.V.

showing

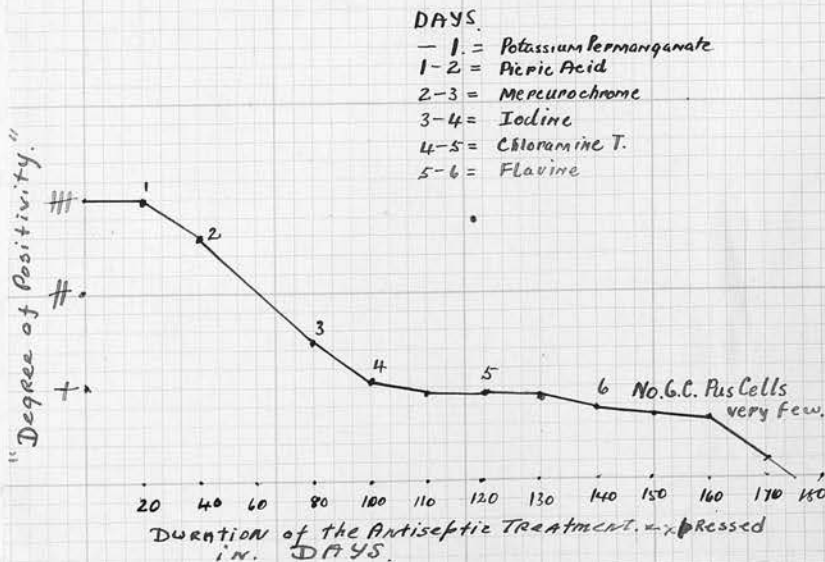
Effect of employing Silver Nitrate at an early stage of the disease.



### CHART No.VI.

showing

further - the influence on the degree of positivity of antiseptics chosen in a definite sequence.



Thus, it is obvious the effect of employing Silver Nitrate at too early a stage of the disease. Note in Chart VI. the gradual, regular decline with treatment until the patient is Gonococci-free and finally cured. Not in Chart V. with the advent of Silver Nitrate the progress is arrested and then the degree of positivity increases under this regime or shortly after another antiseptic, (no matter what you use), is employed. The ultimate result of course should be the same - Gonococci free, but observe how much longer it takes and in addition the probability of damage to the tissues. Chart V. is typical of many Silver Nitrate cases as such, and the practical lesson to be learned here is never to employ this antiseptic as long as Gonococci are present. After that it may be used and, as a matter of fact, is very useful in cleaning up "Pus Cells". Only two cases out of 45 showed a decrease in positivity under the Silver Nitrate Regime.

Colloidal Silver preparations are however much more satisfactory both in reducing the degree of positivity, and also in potentiating the effect of the previous and succeeding antiseptic. In passing we may note that the effects of Colloidal Silver preparations on Ophthalmia Neonatorum were much superior to ordinary Silver preparations, the latter tending to cause a chemical irritation of the conjunctivae.

FURTHER OBSERVATIONS FROM THE ABOVE DATA

From the foregoing it is obvious there is no definite line of treatment regarding antiseptics about which we can be dogmatic. But certain facts have been observed which are useful with particular reference to the Silver preparations. The change of degree of positivity did not bear any direct relationship to the duration of time the antiseptic was employed. Furthermore, from the total series of cases, the bactericidal aspect of irrigation with antiseptics seemed to play a relative minor part. Certain of the antiseptics exhibited in a regular sequence, in a goodly percentage of cases would seem to have facilitated bacteriological "cure". Factors which produced the opposite results were "monotherapy" (too long a period on one antiseptic), improper choice of antiseptic e.g. a powerful astringent (Silver Nitrate) used in the earlier phase of the illness.

The optimum duration period to use an antiseptic was from 2 - 3 weeks. After that the Gonococci seemed to acquire a "tolerance" to the antiseptic in question. Microscopic Examination of Urethral (or otherwise) contents assisted in the choice of antiseptic e.g. the presence of secondary infection indicated an antiseptic which would be efficiently bactericidal yet soothing or at least non damaging to already inflamed and devitalised tissues e.g. Chloramine T.



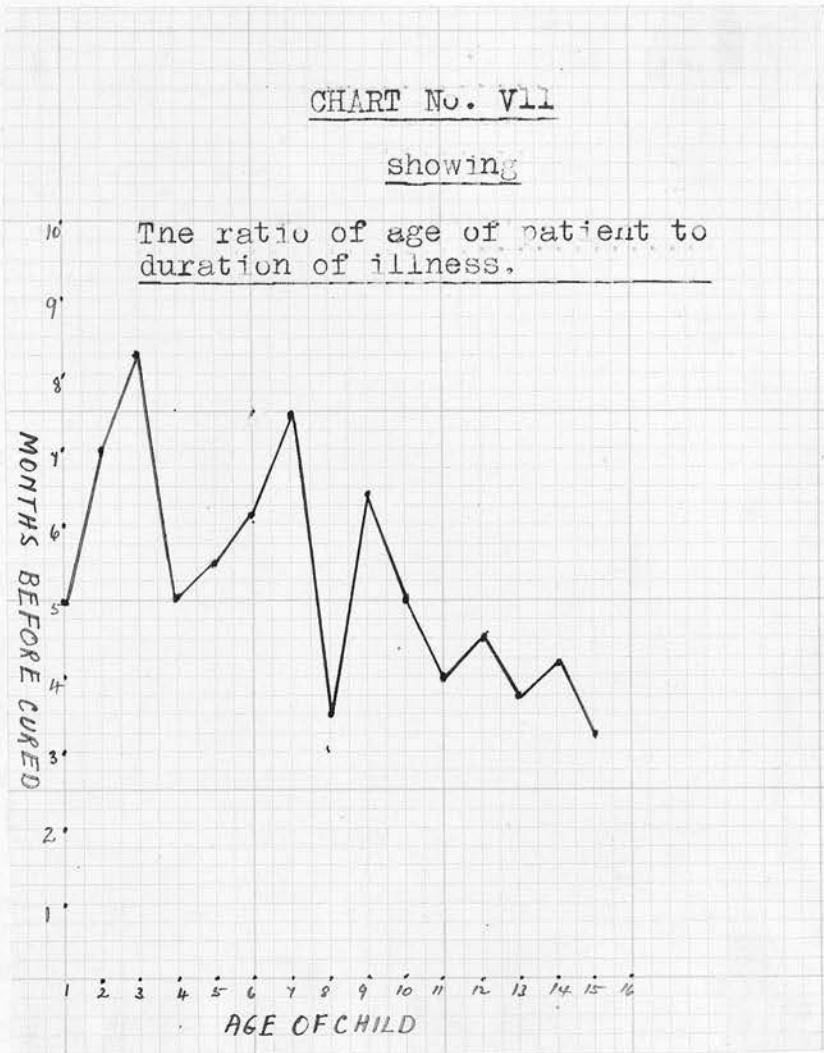
While Picric Acid or Potassium Permanganate have proved highly efficient antiseptics in this review of cases, they should be applied discriminately to obtain their maximum effect e.g. in an obstinate chronic case Potassium Permanganate or Picric Acid, if reverted to, produce a result all depending on the previous antiseptic employed. Powerful astringents, even after they have been withdrawn, still leave their "effects" and, as such, are a decided handicap to the less powerful Potassium Permanganate or Picric Acid. Therefore, to obtain the maximum effect from Potassium Permanganate the patient should previously have been irrigated with Chloramine T. or some such mild antiseptic.

There can be no doubt that irrigation with antiseptics is an important procedure in the treatment of Gonococcal Vulvo-Vaginitis. The fact remains however, that despite the multiplicity of antiseptics at our disposal none have yet met all the requirements of the ideal antiseptic. Thus, we must at present rest content with those available. In the experience of some authorities, certain antiseptics prove highly efficacious but again are found to be equally useless in the hands of others. Probably if one were to consider what I propose to call the collateral factors in Antiseptic Therapy a more general uniformity of results would be obtained by everyone. For example - the Duration of the Infection



is very important - a chronic case is usually very obstinate to treatment. Likewise the Age of the child is no small matter as illustrated by the following chart.

CHART No. VII.



From which we conclude the younger child throws off the infection with greater difficulty than the girl who is approaching puberty with its histological and physiological advantageous changes.

Here we see the average duration of infection in the three years old child is 8.3 months as compared with the fifteen year old one, whose infection lasts on an average 3.2 months.

Other accessory therapeutic measures e.g. Vaccines, Shock Therapy etc., likewise influence the general course of the disease. Further, certain children have what one might say a proclivity towards the disease, the basis of which most likely is lowered resistance - be it local or general.

As we have seen, the optimum period for one antiseptic is 14-21 days. After that the efficiency of the drug seems to deteriorate. Is this due to the tissues or the Gonococcus acquiring a tolerance to that antiseptic in question? Such is quite possible since changing of the antiseptic for a period followed by resumption of the previous one proves beneficial very often.

Therefore, in conclusion with regard to antiseptics we should say that too much must not be expected from any such one. Exercise judgement in selecting your antiseptic, ensure the one you do choose does not defeat its own purpose - be it through over strength or too astringent etc. Supplement this line of treatment with other forms of therapy.

## ACCESSORY THERAPEUTIC MEASURES

A. VACCINES Cole and Meakins<sup>81</sup> in 1907 were among the first to try the effects of Vaccine Therapy. While their results were rather discouraging, one could probably attribute this to the procedure employed in making the Vaccine.

Since that time however, Vaccine Therapy has come to the fore more and more, and at the present day is regarded by the majority of authorities as being a valuable adjuvant. The results however, vary in the hands of different people and one suspects that certain factors which may make all the difference between success and failure should be observed especially: -

(1) Methods of Administration-vary to a certain extent.

Undoubtedly the subcutaneous route is the popular one. This was the one and only method chosen in our clinic and proved quite satisfactory as far as facility, freedom from pain etc is concerned. With other possible routes of administration I have very little experience. The Intradermal route is spoken highly of by Harrison but others again e.g. Hoffmann find it to be of little use. Intravenous administration has been tried by Mac Lachlan<sup>82</sup> with fairly good results but is not universally employed. Probably the risks in children are too great. Likewise the Intramuscular route has not met with general approval, having many

disadvantages especially a marked negative phase, persistent toxic symptoms over a long course, and pain with discomfort at the site of injection.

(2) Type of Vaccine employed of which are a few well-established varieties.

1. The ordinary Polyvalent Vaccine comprising an emulsion of many strains of Gonococci.
2. Sensitised, after the method of Besredka, but otherwise similar to the above.
3. Detoxicated Vaccine prepared after Thomson's<sup>83</sup> method.
4. Autogenous Vaccine usually more beneficial in comparatively recent cases than longstanding ones.
5. Gonococcus Ecto-antigen - originally prepared by White and Winters - who claim good results by giving it intradermally.
6. Gonococcal Bouillon Infiltrate, prepared by Corbus and O'Connor<sup>84</sup> who found it very satisfactory. Its action seems to be mainly a protective one since it stimulates the mucosa of the Genitalia, & also the reticulo-endothelial cells in the skin.
7. Preparations of live Gonococci - autogenous or otherwise - when given intradermally gave good results. Immediate reaction was however more severe - a temperature of 103 degrees being quite common also formation of pustules at the site of inoculation, which on healing left definite scar formation. Two or three intradermal injections given at one sitting were found to be more beneficial, being repeated at weekly intervals and later on at three weekly intervals when the optimum results were obtained.

Preparations Nos. 5, 6 and 7 were not employed in our clinic. Chiefly Detoxicated Vaccine was what one used, because the removal of the toxins enabled larger doses to be given. Autogenous Vaccines were administered in those cases where a secondary infection was superimposed.

Choice of preparation and method of administration are therefore important but in addition one must also consider other factors:-

(a) Study the effect of doseage on the patient and judge the doseage accordingly.

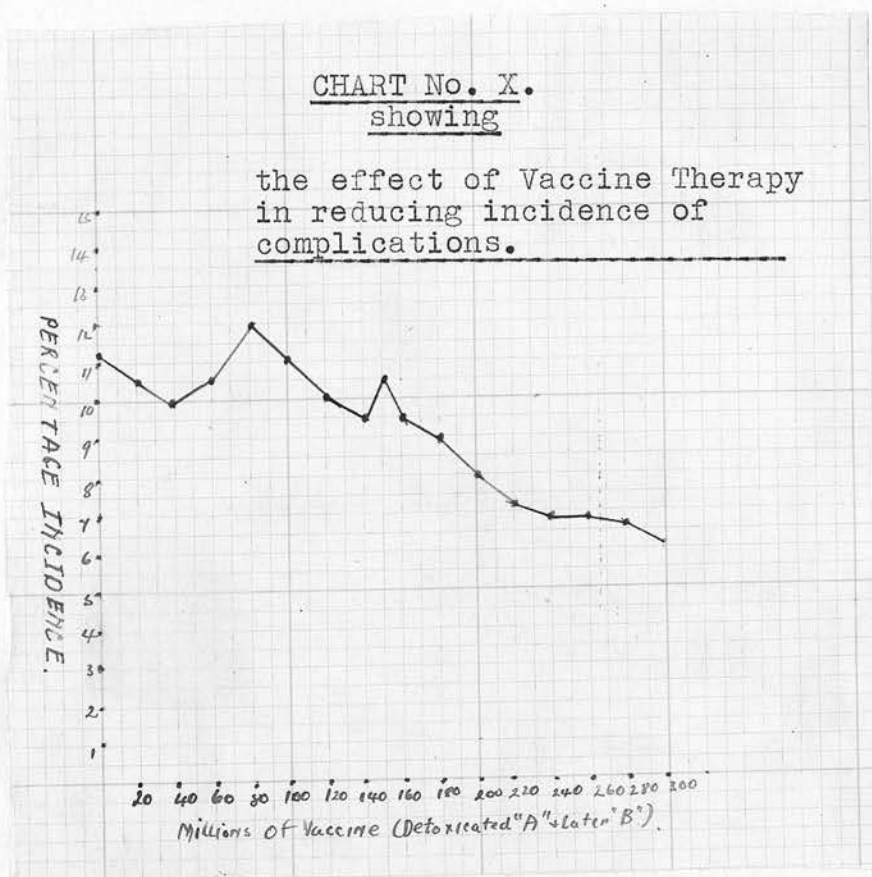
(b) Frequency of administration is also important. No hard and fast rule can be laid down on this matter, all depending on previous doseage and how the patient tolerated it.

(c) The effect of doseage on the local condition.

In other words one must administer Vaccines with discrimination and not stick to hard and fast rules, since a certain type or doseage of Vaccine may agree with one and not with another. We usually employed a Detoxicated Vaccine (made by Genatosan Limited, Loughborough) and started with a dose of 1000 millions organisms for a girl 5 years of age. Doseage was gradually increased all depending on how the patient reacted to the previous dose. Usually a rise of temperature of practically 1 degree which however, subsided after 24 hours, at the most 48 hours, was aimed at. Prolongation of the increased



temperature over 48 hours demanded a reduction in dosage next time assuming no other cause could be found. (Vaccines were usually given twice weekly). Vaccines were given in 78% of our cases and one noticed an appreciable difference in the incidence of complications in Vaccine treated cases. This is well illustrated in Chart X.



From which, one concludes that there is a difference in the percentage incidence of complications in vaccine treated cases. It does not follow however, that once a certain amount of Vaccine is given that one can rest assured, complications will not develop. Far from it, and in fact if a complication has set in, vaccine therapy is of



relatively little use in aborting or even reducing the course of complication. However, we must qualify this statement by saying that much depends on the type of complication. For example, certain authorities have found it useful in the treatment of Gonococcal Arthritis but having had no such cases in our series we must leave it at that. One notes also from the chart that large amounts of vaccine have to be given before condemning its weakness to eliminate complications. One obtains the maximum advantage from the Vaccine by gradually increasing the doseage as tolerated by the patient. In younger children naturally the increase in doseage was more gradual.

From all that has been said one must conclude vaccine therapy has a place in the treatment. This however is not the unanimous opinion. Nabarro<sup>112</sup> and Ronenger have had very disappointing results. Brown found that the average duration of treatment was INCREASED from 18 to 22 weeks in "vaccine" cases but relapses only occurred in 30% as compared with the "non-vaccine" cases. Reith Fraser finds it eminently satisfactory, provided one employs care and discrimination in applying Vaccine Therapy. Daily doses, be they ever so small, give good results. He does not increase or reduce daily doseage after estimating the immunising dose. The latter, he has calculated on the basis that if he gets a marked negative phase the doseage is unsuitable for that child e.g.

<u>Age in years.</u>	<u>Daily Dose in Millions of Detoxicated Vaccine.</u>
- 1	100
3	600
5	1000
10	2000
14	3000

According to this authority, vaccines give a permanent cure and no complications.

Tod who also has a high opinion of Vaccine Therapy gives the following scale of dosage:- Children up to 5 years - 200 millions of the Detoxicated Vaccine twice weekly, gradually increasing the doseage week by week by 200 millions according to the child's age, until 1200 - 1600 millions is reached, then followed by a weekly reduction by 200 millions per dose until <sup>the</sup> course completes itself.

<sup>85</sup> Hamilton after employing Vaccines in 334 cases concludes this form of Therapy has come to stay. His "figures" given below speak for themselves.

	<u>Nos. of Cases</u>	<u>Cured</u>	<u>Uncured</u>	<u>Lost</u>	<u>Percentage</u>
Irrigation	260	158	53	49	60
Vaccines	84	76	5	3	90

<sup>86</sup> Churchill and Soper believe that Vaccines shorten the course of the disease (this was one's conclusion on this matter too). Only they seem to

rely on the Opsonic Index as being a valuable guide to results. To my mind this is not a reliable criterion since it bears no true relation to the severity of the Vaginal Discharge etc.

Among other authorities supporting Vaccine Therapy are Lees,<sup>87</sup> Daken,<sup>88</sup> Butler and Long,<sup>89</sup> Eyre and Stewart,<sup>90</sup> Hamilton and Cooke,<sup>91</sup> Whitehouse,<sup>92</sup> Schmitt<sup>93</sup> Fitzgibbon and Frassi.<sup>94</sup> Again however, a minority still discredit its value e.g. Bruck,<sup>96</sup> Sommer,<sup>97</sup> Sauvage,<sup>98</sup> Hamburger,<sup>99</sup> Jack,<sup>100</sup> Smith,<sup>101</sup> Sullivan and Spalding.<sup>102</sup>

### CONCLUSIONS

As already mentioned elsewhere, the Gonococci do not produce many antibodies in the blood stream for a week or two following the development of the infection. This we see illustrated in the negative Gonococcal Complement Fixation Test in the early stage of the disease.

Since this is the opportune moment for the body defences to successfully attack the organism, and since it fails to do so, seems to be ample reason for the stimulation of the tissue defences by artificial means. This then, is accomplished by Vaccine Therapy and would appear to be the rational method to attack the problem. Theoretically speaking, this line of treatment should kill off the Gonococci immediately sufficient antibodies have been created, but unfortunately such is not the case. Whether it is because the perfect Vaccine has not been discovered or no, one cannot be certain. We do get a certain

length however, in reducing the infection. Most authorities now admit that this form of therapy, which is easily administered, relatively painless, and harmless, is definitely beneficial to the infected child.

Personal experience has led one to use the Detoxicated Vaccine "A" in the early stages and later, when secondary infection is present, Detoxicated Vaccine "B." If the latter fails, then occasionally an autogenous preparation has proved successful.

Hamilton's experience clearly proved that in itself Vaccine Therapy is not enough to produce "Cure". It is, at the best, an accessory factor in the treatment. It reduces the virulence of the disease, tends to prevent the occurrence of complications, and would appear to definitely shorten the course of the illness, but does not seem to have much effect on complications already present.

#### B. Serum Therapy

We have had no personal experience with the above. Herrold and Hoffmann<sup>103</sup> tried it out in a series of 40 cases. Their results showed that 10% had Serum Reaction (sickness, joint swelling etc); many had urticarial rashes not unlike Erysipelas over the site of inoculation; some showed beneficial results in controlling the immediate clinical picture; complications showed a varying degree of improvement; skin tests showed an increased antigenotoxin content

in the Patient's serum. They concluded that the results would have been more satisfactory had the antiserum been of a more concentrated form.

Serum Therapy would therefore seem to have its advantages. It would appear to have the advantage over Vaccine Therapy in the treatment of complications but one can see numerous disadvantages in Herrold and Hoffmann's results.

(a) Serum Reaction - a fairly high percentage show serum intolerance and thus can assume an alarming degree of danger if carried out on an extensive scale.

(b) Skin tests - showed the serum antigenotoxin content to be increased but is the antimicrobial powers of the serum increased?

Admittedly an increased systemic resistance is very desirable, but there seems little use in stimulating systemic resistance if the site of toxin production is left unharmed i.e. the Gonococci in the Genital Tract and elsewhere.

(c) Protein Shock and Anaphylaxis We have dealt with Serum intolerance but since the above authorities conclude that a more concentrated form of Serum is required one would like to ask - is the line of treatment worth the risk of incurring Protein Shock, Anaphylaxis etc. in view of the following facts?

- (1) Gonococcal Vulvo-Vaginitis is seldom a fatal disease.
- (2) The numerous other and reliable methods of treatment at our disposal
- (3) The possibility of having to administer serum later in life for a more urgent illness (e.g. Scarlet Fever or Diphtheria). with possible grave sequelae.

#### C. Chemotherapy via the Blood Stream.

The administration of alkalis we have seen forms part of the routine treatment in every case, since an alkaline urine is unfavourable to the existence of the Gonococci apart from the diuretic action.

Antiseptics introduced via the Blood Stream were never employed in this series of cases so that one cannot discuss their merits. However, the



fact that they are not used much nowadays would warrant their lack of success as an auxiliary line of treatment.

D. Electro - Thermic Cautery:- has been employed in America with good results. One clinic report:-

64% cessation of discharge (which however does not imply cure).

23% marked improvement.

13% varying improvement.

It would seem to be more beneficial in the more chronic case. No after effects such as scarring, stricture formation, post operative menorrhagia, dysmenorrhoea, were reported.

E. Non Specific Protein Shock Therapy - was employed in 36.3% of cases and the results reveal the surprising fact that the average duration of the case in question was 1.25 months more than those cases where Shock Therapy was not employed. This does not necessarily imply protein shock therapy prolongs the illness - possibly these cases in which it was employed were proving to be unusually obstinate cases. But we can safely conclude that the results of this line of treatment did not justify the protracted trial it did get.

Different preparations were employed, the chief of which were :-



- (a) "Aolan 3" - 5 ccs. - Intramuscularly, once weekly.
- (b) "Edwenil" - 1c.c. gradually increasing to 2 c.cs. twice daily.
- (c) Sterile milk - in doses similar to "Aolan"
- (d) Nucleic Acid - orally
- (e) "Arthrigen" - a combination of Urotropin and Gonococci - given Intravenously.

Of the lot Arthrigen was by far the most satisfactory, No form of Shock Therapy was of much use in a straight forward Gonococcal Vulvo-Vaginitis case and even in "complications" their value was doubtful.

#### F Other Methods.

1. Ketogenic Diet. This was tried out by way of an experiment on only two cases. The rationale of this "experiment" was based on the fact that Ketogenic Diet is somehow of great value in Pyelitis especially that of the B.Coli type. Each child was kept on this diet for 4 - 6 weeks but this was abandoned because apart from the fact that the children lost weight and the general health gradually got worse there was no improvement in the condition. Personally one concludes that failure to improve under this treatment is not to be wondered at since (1) we have just mentioned Alkalis are given to render the urine Alkaline which is detrimental to the existence of Gonococci. A Ketogenic Diet is given to produce purposely an acid urine. Ofcourse, again, the urine reaction will be hyperacid under a rigid Ketogenic Diet, which may be as antagonistic to the Gonococci as an alkaline one. (11) This only applies to the urine and therefore can have little or no effect on Vaginal or Cervical Involvement.

11 Infra Red Ray. This was tried out in a series of ten cases. The "longwave" which has a penetrating depth of approximately two inches was first employed - the ray being directed through the suprapubic region Abdominal Wall at an angle of 45 degrees with the object of focussing it on the infected cervix. The "Short wave" with its penetrating depth being only a matter of a few millimetres was applied to the Vulvar region. Exposures lasted half an hour at each

"sitting" and occurred twice daily. A trial of three weeks was given and then results were compared.

Results One must admit there was a slight but definite improvement clinically and bacteriologically. The improvement was more marked in these cases which exhibited no Gonococci i.e. where a slight mucoid discharge containing pus cells existed. Unfortunately at the time we were experimenting with this Ray treatment there were no available cases of complications apart from more or less slightly involved "Cervices". We should very much have liked to try it on a Salpingitis, for the simple reason that a young woman in Hospital at the time with a Salpingitis showed a decided and rapid improvement when treated with the Infra Red Ray as already outlined. So that in conclusion we maintain that this line of treatment, applied to the infected child who suffers no ill effects (which is unlikely) from exposure to the ray might be worth an extended trial

Unfortunately we have not had experience with Malaria Therapy as applied to Gonococcal Vulvo-Vaginitis but we quote the following, since it would seem to be worthy of a trial in the opinion of certain authorities notably COURTIN<sup>104</sup> who maintains that it shortens the course of a Gonococcal Vulvo-Vaginitis illness, is particularly useful in the chronic case but should always be used in conjunction with "local" therapy to the Vulvo-Vaginal region. Spiethoff is of the opinion that it only affects Gonococci in the deeper tissues and is in complete agreement with Courtin that local treatment is essential to clear up the superficial tissues.

However, those who do not believe in Malaria, point out all its disadvantages re the Heart in particular, and moreover maintain that some children tolerate Malaria very badly and frequently with serious results.

COMPLICATIONS

Analysis of the records at this clinic from 1922 - 27 reveal a higher incidence of complications from Gonococcal Vulvo-Vaginitis than in the last five years.

The incidence of the above varies in the hands of different authorities. The following percentage figures gleaned from various sources are sufficient to explain the point in question.

<u>Complications</u>	<u>Brown at Guy's Hospital</u>	<u>Children's Medical Home</u>	<u>Tod</u>	<u>Brunet</u>	<u>Titus &amp; Notes</u>	<u>Lees</u>	<u>Own Results.</u>
Urethritis	12.2.	67.0	-	-	-	98 +	99 +
Bartholinitis	-	-	-	-	-	-	0
Cervicitis	-	4.0	-	-	-	-	16.6
Endometritis	-	} 1.3.	-	-	-	-	0
Salpingitis	-		-	-	-	} 5.5	} 2.7
Pelvic Peritonitis	1.5	-	-	1.2	.07		
Eye	3.0	2.5	-	.6	0	8.3	3.8
Arthritis	1.5	1.3	1.5	0	-	-	0
Proctitis	4.6	4.0	-	.09	0	2.7	2.0
Warts	-	-	-	-	-	-	1.0
Cystitis	-	5.0	1.4	-	0	.9	1.3
Vulvar Ulcer- ation Non Specific	-	-	-	-	-	1.8	2.4

Acquired Syphilis of the Vulva was observed in 1% of cases in our series.

One would like to point out a few outstanding features from the above figures.

URETHRITIS A very marked divergence of views is evidently held here. Brown's figures are very low - more in keeping with those of Reith Fraser who maintains the infection proceeds no further than the urinary meatus. Brown however, admits that the urethra was not examined on every occasion in all cases, and one agrees that Fraser's suggestion (that more frequent Rectal examinations would reveal a higher incidence of Proctitis) if applied to urethral examination would lead in all likelihood to an increased incidence in positive Gonococcal urethritis being diagnosed. Anatomical factors render the urethra particularly vulnerable to Gonococcal Infection spreading from the Vulva, Vagina etc. As will be seen from the figures quoted, practically every case showed urethral infection and the "specimens" for Bacteriological Examination were taken from within the urethra, not from the meatus. Hence one agrees with Norris, Watson, and Moorhead that urethritis should be regarded as part of the clinical picture just as Fraser regards

#### PROCTITIS

as a part of the clinical picture. Kaumheimer,<sup>105</sup> Valentin<sup>106</sup> (who found 38% positive) support Fraser in this belief. Kidd, Simpson, Watson and others believe that the degree of Rectal Involvement is nothing like the figure given by Fraser, who places it as high

as 90.4% With Watson among others, we agree, and Rectal Examination (clinically and Bacteriologically) was carried out thoroughly on each case.

### CERVIX

One is rather impressed with the degree of cervical involvement. Granted, most cases showed only a slight infection, but fortunately were caught at this early stage. The explanation of such a relatively high incidence is not far to seek. Vaginal discharge cumulates behind the Hymen - irrigation no matter how carefully performed, is bound to carry a certain amount of infected "wash" against the Vaginal Cervix prior to the "backflow". Absence of menstruation also "encourages" involvement of this region from both the mechanical and physiological point of view. More recent investigation has cast a new light on this question. The immature uterus in the child is much more sensitive than previously thought to be. The effect of forcing the irrigation tends to carry the infection upwards not merely from the mechanical point of view. This stimulus (mechanical and thermal), sets up retro-peristaltic movements of the uterus and tends thus to further upward spread. And, as Vogt<sup>107</sup> points out, the cervix comprises the greater part of the immature uterus. To go a stage further - there is no Internal Os in the uterus at this age and thence a Tubal Infection is always possible since the Tubes are patent (as has been recently shown). Our very few cases of Tubal involvement were of a very mild type and none were fatal. This contrasts



markedly with Galvagno's records where the mortality rate was 20%. Despite this theory however, many still hold that the infection travels by the Blood Stream.

The above explanation thus shows the possible dangers of over zealous irrigation. Williams emphasised this long ago, and recently has shown that "the cervix is involved, often in the acute phase practically always in the subacute and chronic stage".

The above were the chief complications observed regarding frequency of occurrence but certain others while less common were no less serious.

#### EYE INFECTION

Practically all our cases occurred in young infants and naturally the question arises as to which came first. Presumably the eye condition was the origin but two cases showed a history where Vulvo-Vaginitis was definitely the original focus. Hamilton reports an incidence of 1.2% in his series of cases.

CYSTITIS - fortunately those cases were very few, of a mild nature, and cleared up without much difficulty.

OTHER COMPLICATIONS Skin lesions around the involved region, especially of the erythematous type due to irritation from the vaginal discharge, were numerous, but of a mild degree. Adenitis - Inguinal in type during the acute phase of the illness occurred in 60% of cases and was transitory.

ARTHRITIS - not very common but Pollock has reported 3 cases.

"The Abdominal Picture" - as reported by Anwyl Davies



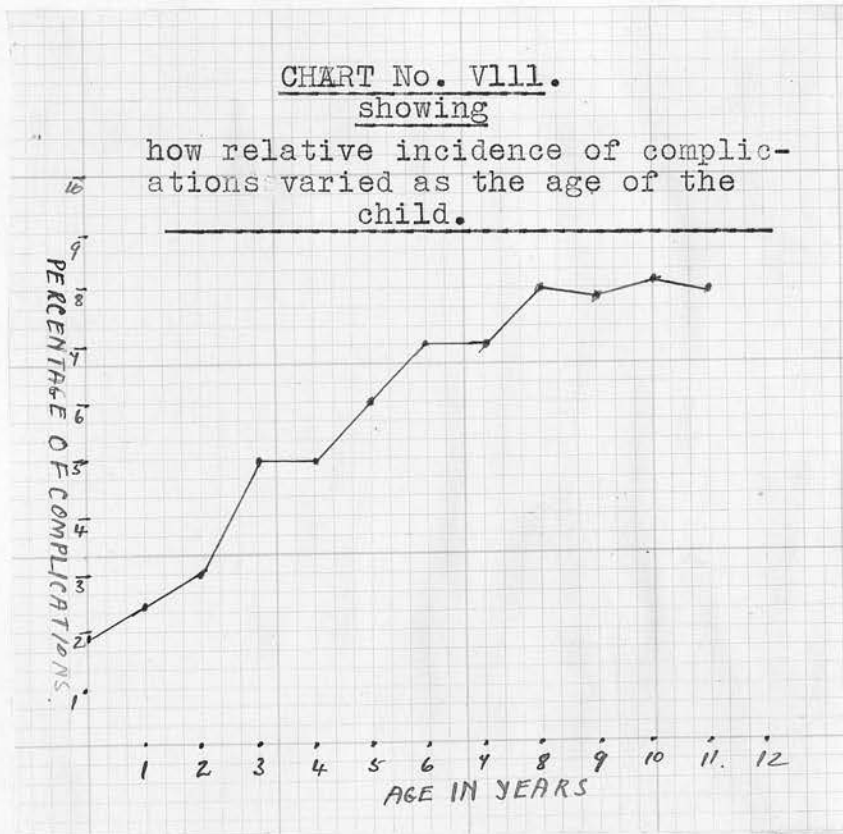
is not often seen, and especially in children less than two years old since the cervix is very immature at that age. The child complains of vague abdominal pain, looks ill, and has the abdominal facies - rather pinched, pale etc. I have had no experience with this type of case. Warts (Condyloma Acuminata) were occasionally seen in unhealthy and dirty children.

Tubal Infection may lead to a Peritonitis but, typical of Gonococcal Peritonitis, is of the localised type, and in the case where it is a sequel to a Tubal Infection, naturally is confined to the region of the Tube in question. My incidence of this complication as seen is very small, but if one looks at it from the point of view that it is a Blood distributed infection, then this complication must be regarded as a relatively serious one. Although the condition is not very frequent, Jung, Carpenter, Bidwell, Baer and numerous others have reported cases.

#### FURTHER PERSONAL OBSERVATIONS

The total incidence 17.4% compares favourably with that of the previous five years at this clinic. (21.2%) - Urethritis is regarded as part of the clinical picture - Proctitis etc, as complications. To what extent natural resistance accounts for the improvement is difficult to say. Vaccine Therapy has undoubtedly played a most important part. Analysis of the cases shows that Vaccines have been employed much more in the past 5 years than previously.

Age too has an important bearing on the type of complication met with e.g. Eye infections are commoner in the infant group than in girls say 9 - 10 years of age. Also the incidence of complications would seem to vary as the age. Chart Vlll. illustrates the point.

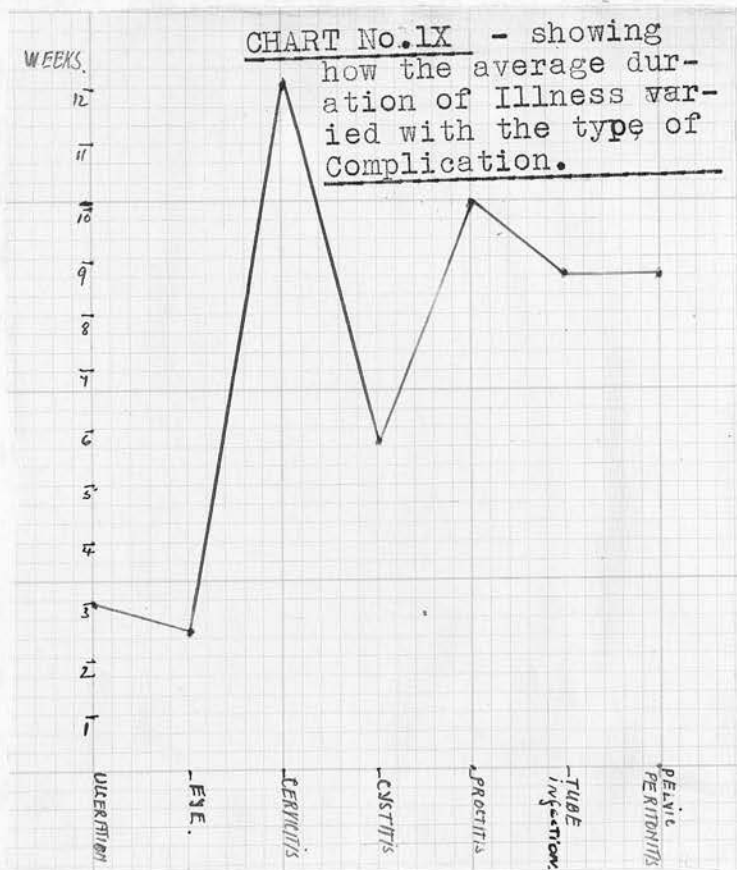


From which one deduces that from the sixth year of life onwards the highest percentage of complications occur.

Complications naturally tend to prolong the duration of illness. The average duration per case, free from complications, was 4.9 months; that of the case showing complications 5.8 months. Taking each case individually certain cases tended to show

more obstinacy than others and it was noted that, allowing for other factors, (e.g. general resistance vaccine therapy etc.) a more or less definite relationship between duration of illness and type of complication could be found. e.g.

CHART no.1X.



I have already referred briefly to the effect of Vaccine Therapy in reducing the incidence of complications. This will be discussed in fuller detail later, but in passing, we are very doubtful if Vaccines are beneficial at all in curing an already existing complication. By far the most disappointing results were with Cervical and Tubal involvement.

Here they seemed quite useless as the rate of recovery, duration, and severity of the condition were not minimised when Vaccines were given, which preparations varied from the "Ordinary" Detoxicated to the Autogenous Vaccine.

To further emphasise the point one would carry out Cervical examination. Apart from its persistent nature this complication is liable to promote involvement of the Genital Tract further up. Our few cases of Tubal Infection showed Cervical Involvement but despite attentive measures to the latter, Salpingitis ensued. This latter condition was never acute in any of the cases and gave no trouble regarding Differential Diagnosis from Appendicitis.

The Influence of Acquired or Congenital Syphilis was very interesting in those few cases which occurred. One is inclined to believe from personal observation, that the presence of Syphilis seems to potentiate the virulence of the Gonococci. Ofcourse this is merely hypothetical but those cases in question showed a prolonged duration of the disease, liability to complications etc; which made one wonder if some kind of devitalising factor was present apart from what is known as general debility. Admittedly the Spirochaeta Pallida must devitalise the tissues but does it directly, or indirectly by producing a toxin, inhibit that "something" necessary for the stimulation of the tissue defences. To illustrate

the point: - A little girl age 16 months with an acquired Syphilitic infection plus Gonococcal Vulvo-Vaginitis. As long as she is on Antispecific treatment her Vaginal discharge is much reduced both in positivity for Gonococci and <sup>6</sup>numers of pus cells per Microscopic Field. Put the patient on her "month's rest" from Antispecific treatment, and there was an appreciable change for the worse in her Gonococcal Vulvo-Vaginitis condition, shortly afterwards. This happened more than once in this case and is worth noting. Was it the beneficial effect of Arsenic as a general stimulant or as an antiseptic substance?

S T A N D A R D   O F   C U R E

This varies in the hands of different people, which implies an absence of definite criteria to guide one. To quote a few authorities will illustrate the great divergence in views existing at the present day.

A. Reith Fraser.

- a. Three consecutive fortnightly smears.
- b. If negative, cultural examination, of Vulva, Urethra, Vagina, Cervix and Rectum.
- c. If negative treatment is stopped.
- d. Patient reports in three months time, and if tests satisfactory she is discharged cured. The trial tests are preceded by a provocative injection before the final ones..

One observes (a) he does not place much faith on the value of Gonococcal Complement Fixation Test.

(b) Urethral examinations are a prominent feature in his tests for cure despite the fact he regards Urethral Infection as being relatively uncommon.

(c) The thorough and rigid tests which the child must pass satisfactorily before she is discharged as cured.

B. Brown.

a. Continues treatment for 4 - 6 weeks after apparent clinical and bacteriological "cure".

b. Following which treatment is stopped; films and cultures are taken from urethra Vagina and Cervix at 7, 10 and 14 days interval over a period of three months



i.e. at least 6 tests during the observation period.

c. Prior to the final tests a provocative dose of Polyvalent Vaccine is given.

C. Norris

a. Three consecutive fortnightly smears after apparent clinical "cure" and cessation of treatment.

b. Prior to the last set of tests, he employs chemical irritation as a provocative procedure.

D. Mac Nicol<sup>110</sup>

Has the child if possible under observation for one year during the first three months of which the child should (1) be clinically well and

(2) reveal no pus cells and Gonococci.

She does not employ provocative methods.

Our criteria for tests of cure are more or less on the following basis.

a. Cessation of treatment three weeks after clinical and bacteriological "Cure".

b. Three successive weekly examinations, clinically and bacteriologically.

c. A repetition of "b" at monthly intervals instead of weekly periods.

d. A provocative dose of Polyvalent Vaccine (doseage varying with the age of the child e.g. a girl of 11 or 12 years would get 200 - 300 million organisms) is given in all cases.

e. Successful results from the above are regarded as satisfactory from the point of view of cure.

CONCLUSIONS

Since we are dealing with a disease for which we have no definite line of treatment which will lead to absolute cure in every case, and since the disease shows a tendency to relapse, the standard of cure must essentially be a high one.

Admittedly, we have not a universal code of laws laid down which demand fulfilling in all respects. But although this is lacking, each and every authority adopt the following as a working basis:-

- a. Absence of Gonococci, other Pathogenic organisms, or pus cells.
- b. Reducing to a minimum the possibility of permanent damage especially if the cases have been attended by complications.

They aim at:-

- a. Satisfying themselves the patient is cured.
- b. Eliminating the possibility of relapse.
- c. Protecting the children from possible sequelae as a result of the disease.
- d. Inconveniencing the patient as little as possible.
- e. Minimising the period under treatment and observation, within reasonable limits of safety.
- f. A practicable "workable" Standard of cure.

Absolute cure, or as near to that as possible is essential. The danger of "Carriers" and cases of relapse speaks for itself. Regarding the

latter, we were impressed with MacNicol's long period of observation as a criterion in the test of cure. Was it justified? Her incidence of relapse would seem to justify it - the figure being 25.7% as compared with Brown's 54%. Fraser's figures were very low-4.9% of cases. One must bear in mind however, his standard of cure was very high and although of a shorter duration, the tests were more rigid.

As already said, the standard of cure varies in the hands of different authorities; their technique differ in various respects, some of which perhaps may have an important bearing on the results. For instance, MacNicol did not employ provocative measures, to any extent. Probably if she had done so, her percentage of relapses might have been much lower. But despite all rigid precautions, relapses will and do occur. Often the fault lies with the patients in that they fail to attend for treatment after discharge from hospital, but are still instructed to attend periodically, usually twice weekly. This was our experience in a few cases, which accounted for a goodly percentage of our relapses. The danger is obvious, since although, apparently cured, they still continue to harbour a Gonococcal discharge which may result in transmission of the disease. In other words they are "Carriers".

Our incidence of "relapses" was 8.6%, a very satisfactory figure when one considers a large

percentage of them was due to defaulting from treatment as "outpatients". This group accounted for 80% of our relapses.

The standard of cure has also an important bearing on that period of time from the initial symptoms until the time of discharge. If the standard of tests for cure is low then this period will be of a shorter duration. Excluding those exceptional cases, we are a bit sceptical of those results where children were treated and cured in the space of a few weeks e. g. Maggiore's cases where, on a certain line of treatment, previously mentioned, the patient<sup>was</sup> discharged cured in a very few weeks.

Herewith is appended a few figures from different sources, correlating the duration of attendance by the child to the incidence of relapses.

<u>Authors</u>	<u>Average Duration of Attendance until discharged cured.</u>	<u>Incidence of Relapses</u>
Brown	15.75 months	54%
Reith Fraser	8.5 months	4.9%
Lees	7 months	8.7%
Childrens Medical Home.	7.75 months	-
MacNicol	17 months	25.7%
Own Figures	6.3 months	8.6%

So that the duration of the illness bears no direct relation to the possibility of relapse.

Presumably more important factors are:-

- a Methods of treatment employed, and
- b the standard of cure adopted.

This is borne out by the figures obtained by Lees and us in the same Clinic at different periods.

We regard Reith Fraser's standard of cure better than any other. Both "duration of attendance" and incidence of relapses bear out this observation. Naturally such a statement is open to criticism. Perhaps the number of cases he reviewed were not extensive enough; may be he was fortunate with the type of case encountered i.e. early cases brought to medical notice before the disease had obtained a firm footing; or again may be, many of his cases had a very good natural general resistance and were thus able at least to prevent the occurrence of intermittent infection which perhaps had something to do with reducing the virulence of the disease; or again, if one dare enter into such problematic spheres, may be the average strain of Gonococci were of a less virulent type. Doubtless those and many other points would be advanced by others in attempting to explain away his satisfactory results.

The whole problem of tests for cure in Gonococcal Vulvo-Vaginitis is in a state similar to Gonococcal Infection in the adult female i.e. very unsatisfactory. Obviously there is scope for improvement in this very important problem (this will be discussed later).



GENERAL DISCUSSION

Throughout this dissertation, we have repeatedly emphasised certain salient features. This disease is most unsatisfactory both from the diagnostic and the treatment points of view.

The intractibility of the condition shows up our therapeutic efforts in rather a bad light and emphasises the lack of, and the great need for, a line of treatment which would be uniform and universally adopted. Attempts have already been made to emphasise the therapeutic difficulties with which we have to contend and therefore, contribute to making it a more or less intractible disease e.g. the difficulty in gaining access to the Gonococci in the glands and submucosal tissue, and the unfortunate state of affairs which exist anatomically and physiologically at that age in the young patient's life. In addition however, we are of the opinion that a very narrow margin exists between the bacteriotropic and organotropic strength of any antiseptic employed in treatment. Admittedly, the strength of the antiseptic in question need not be very great but there must be a minimum lethal strength for the Gonococcus, as for any other organism.

Moreover, as we have pointed out from personal experience we seldom found the Gonococcal Complement Fixation Test positive to any satisfactory degree in the early phase of the illness. Which all goes to prove the natural resistance of the patient



expressed in terms of "Antibodies" is not all that could be desired to reduce or even eliminate the Gonococcal disturbance. If we could only "bridge this gap" and raise the resistance powers of the patient then it might be a different story. One assumes not unreasonably, that this is "THE" time above all, when the Gonococcus entrenches itself firmly in tissues. How are we to combat this critical period? At present, efforts to tackle the problem locally have not been very successful. The ratio of tissue devitalisation (and may be destruction in some cases) to killing off the Gonococci in the affected area, is not definitely known in our present state of knowledge. We are not in a position to say that the latter outweighs the former. After all, we are not dealing with fully developed, strong, resistant tissues, but that of an immature nature, being under-developed and therefore in a more "delicate" state.

The above hypothesis is not intended to deprecate the local application of antiseptics as a method of treatment. It is merely a personal view, and we are of the opinion that this form of treatment (i.e. antiseptic therapy) would be more efficacious at a later stage in the disease as the chief line of attack when it would be carried out more frequently, than in the first few weeks of the disease. It would appear to us that the delicate mucosa already subjected to organismal irritation is further devitalised by chemical irritation. For no matter how gently we apply the antiseptic, and how

dilute it may be, further irritation is almost bound to ensue.

Vaccine Therapy has not its established place in the treatment of Gonococcal Vulvo-Vaginitis. Why does it not play an even more prominent part? If Antibody formation takes such a long time, relatively speaking, to attain an adequate level as a means of aborting the disease, why cannot vaccines stimulate the process as it does in numerous other diseases (e.g. Cystitis, Staphylococcal Skin Infection) . It is a difficult question to answer, but comparatively recent work by Thomson and others, is beginning to shed light on the matter. We have previously alluded to the question of different Gonococcal "Strains". While this may not be entirely true perhaps there is something to be said for it. Or is it the question of an attenuated virulence of the organism? At any rate the "Soil" cannot put up the same resistance to the "Seed" in the child, as compared with the adult. And yet it is not any more severe than in the latter. Are we dealing with a different strain of Gonococcus or is it merely an attenuated form of one, and only one strain? We are inclined to believe that both factors are equally important since such delicate "Soil" cannot offer much resistance, especially Natural Specific Resistance, although some contend such does exist.

Thomson has definitely proved to his satisfaction that there are different strains of Gonococci, and has prepared a Polyvalent Vaccine accordingly. This has not proved sufficient to check the entrenching of the disease in the early phase. Wherein lies the failure? If we could but isolate that specific antagonistic substance and administer it in sufficient doses, then we might be able, not only to shorten the duration of the disease, but even prevent its occurrence. So that our failure would seem to lie in Vaccine Therapy - the fault lying either in the preparation of the Vaccine or the administration-or our failure so far, to realise the properties of the "Seed". With regard to the preparation of the Vaccine it is difficult to understand wherein the fault lies, since Autogenous Vaccine Therapy is relatively successful in the treatment of other diseases. Moreover an Autogenous Vaccine for Gonococcal Infection is sufficiently "specific" in that, such a vaccine will not benefit other infections to any extent, even in cases where the disease is due to organisms closely simulating the Gonococcus e.g. Micrococcus Catarrhalis. And yet again, Vaccine Therapy in general has proved to be so successful in the treatment of other diseases such as Cystitis, Staphylococcal and Streptococcal lesions, that one cannot understand why it proves so unsuccessful in the treatment of Gonococcal Vulvo-Vaginitis.

With regard to the administration of

the Vaccine being at fault the route employed would not seem to be the cause,,since Subcutaneous, Intravenous, Intramuscular, and Intradermal routes have all been attempted without satisfactory results. Perhaps we have not yet attained sufficient knowledge on the question of doseage and frequency of administration. ( See Reith Fraser - page 103)

The following statistics gleaned from various sources illustrate how unsatisfactory is the present state of affairs regarding duration and intractability of the disease.

<u>Author</u>	<u>Cured</u>	<u>Still Attending</u>	i.e. <u>Percentage Still Attending</u>
Tod	30	19	63.3
Lees	87	59	32.9
Brown	46	48	47
Own Figures	74	31	33.7

The above figures do not include such cases as Defaulters, patients who died etc. Our figures compare favourably with those of Tod but as shown, are far from satisfactory.

We have already referred to the question of Specific Natural Resistance with regard to certain authors doubting its existence. Such is a difficult matter to discuss but we are inclined to share the view of those who question it. Specific Natural Resistance, however, is quite a different matter from

General Natural Resistance. Gonococcal Vulvo-Vaginitis fortunately is a self limiting disease, and seldom exists after puberty. Nevertheless, it may exist for years before that period in life, and Epstein, quotes cases where it existed from Infancy until those children were 10 years of age. Fortunately this is the exception rather than the rule, but even so, Natural General Resistance must be raised to combat the infection, or at least to prevent inter-current infection. The importance of fresh air, sunshine, and nourishing diet was clearly illustrated in the cases under review. 70% of those children came from homes where economic factors or otherwise, prevented them from obtaining those features already mentioned. Under Hospital Regime the response to healthy environment and good feeding was remarkable - the following fact were notice.

The more severe the Gonococcal Infection the slower was the increase in weight. Not one child lost weight even temporarily or remained stationary, but each and every one showed a varying degree of increase in weight. The effect of any line of treatment with the exception of Vaccines did not arrest the progress of weight increase. Vaccines, in moderation, caused no detrimental change, but, when pushed, tended to cause a very much slower increase in weight. Discharge from Hospital saw, in many cases, a definite set back to the maintenance of weight increase. General physique had no favourable bearing on the



development case. Its importance lies in the warding off of intercurrent infection, which is not uncommon, in Gonococcal Vulvo-Vaginitis e.g. we found Lobar Pneumonia, Broncho-Pneumonia, Scarlet Fever, Measles, Chickenpox all occurring, apart from numerous minor ailments. (Both cases of Pneumonia terminated fatally).

Natural General Immunity is unknown in Gonococcal Infection. Likewise there is no such thing as permanently acquired immunity.

We propose to look at the question of General Natural Resistance from another angle. The coexistence of Gonococcal Vulvo-Vaginitis and Syphilis in one of our young cases has already been alluded to. It was pointed out how on arsenical treatment, the Gonococcal condition improved, withdrawal of this drug leading to a set-back in the progress of Gonococcal Infection.

How did the arsenic act? It was not likely to be a local beneficial reaction. Presumably it acted as a tonic - which incidentally is a very vague term. Arsenic is stored in the liver, but if very small doses be given the detrimental effects on this organ are markedly reduced. As a matter of fact, small doses of this drug have a beneficial effect on the liver which plays an important part in body metabolism. So that, "a healthy liver implies healthy metabolism". This is seen in Syphilitic cases, who experience usually a feeling of well being when on



Arsenical treatment. So that body metabolism would seem to play an important part in Natural General Resistance. In addition, the "tonic" effect of arsenic may be explained by its stimulating the formation of Agglutinins, Lysins, and Antibodies of low specificity (e.g. as seen in cutaneous Tuberculous lesions), which means increased tissue resistance. Those Agglutinins however, cannot differentiate Gonococci from Micrococcus Catarrhalis, Meningococcus, and members of this group. Hence this form of attack, presumably is to a great extent "nullified" by such organisms as Micrococcus Catarrhalis which occur normally in the Naso-Pharyngeal tract.

So that, at the present time, our Therapeutic knowledge shows us in rather a bad light. We suggest that more should be made of Vaccine Therapy which demands further investigation in that line. How can we explain our failure in this line of treatment? Is it (1) some intrinsic property of the Gonococcus with which we are not acquainted; (2) some fault in the preparation of the Vaccine; (3) error (or errors) regarding the method of administration?

With reference to "Method of Administration" - such in our opinion is not THE cause of failure, since Vaccine Therapy in other diseases is eminently satisfactory, when administration is carried out at regular intervals and always by the same route i.e. subcutaneous, which was the method employed by us.

The preparation of the Vaccine - we regard as an important point. To a large extent it depends on a thorough knowledge of the organism in question. Since we have pointed out that there is probably some intrinsic property of the organism still unknown to us, then, until that is discovered, an efficient Vaccine cannot be prepared.

In Gonococcal Vulvo-Vaginitis, we are primarily concerned with lesions of the Mucosa. Mucosal lesions can occur elsewhere in the body, for example, the common Streptococcal Sore Throat, but the difference between the former and the latter lies in the fact that the body can generate a would-be specific resistance, expressed in terms of antibodies, which can overcome the infection in a considerable short space of time in the case of the latter. Now in Gonococcal Vulvo-Vaginitis, we have already seen that antibodies are not present in the blood in sufficiently large numbers until about the fourth week from the onset of the infection when the Gonococcal Complement Fixation Test becomes positive. This has been explained as being due to the fact that the infection is very superficial (in the early stage of the disease), and it is only when the infection becomes submucosal that antibodies in relatively large numbers are produced. In the case of Streptococcal Throat however, the infection is superficial for an even longer period of time than in the case of a Gonococcal Mucosal infection, and yet the

antibody production is much more quickly in evidence than in the case of Gonococcal Vulvo-Vaginitis.

If we fail with Vaccine Therapy to find a solution to the problem why is Serum Therapy not more employed? For example, in lesions commencing in the Mucosa, Serum Therapy at the present day forms the chief line of treatment e.g. Diphtheria, Scarletina etc.

From which conclusions, it is evident we believe in general measures rather than local. The latter have their place, but we are not dealing with the simple problem of "flushing out" or killing off of Gonococci on a mucosal surface. Until we can get more knowledge on this matter - especially pathological, biochemical changes in the local tissues - it seems reasonable, one should attack the infection via the Blood Stream.

Our difficulty lies in the preparation of a more satisfactory vaccine, but to us this form of therapy would seem to more logical for the following reason:- We aim at keeping the parts dry by powder insufflation etc. after irrigation and other measure. But during irrigation we have mechanical plus chemical, superimposed on organismal irritation which, we assume not unreasonably, promotes further irritation and devitalisation of the tissues.

As we mention elsewhere, we do not

disapprove of irrigation. We are simply endeavouring to point out that too many authorities at the present day regard this as the one, and only one, line of treatment.

Moreover, modern Therapy tends towards general rather than local treatment e.g. treatment of Furunculosis with vaccines and other general measures. By this, however, we do not imply neglecting the local lesion completely, but are simply emphasising the former.

Further we would like to stress the importance of raising General Resistance, since it would seem, in the absence of Acquired Specific Resistance at the present day, and with the failure of local antiseptic therapy, the disease when left alone is ultimately conquered by the patient's resistance. How this comes about we do not fully understand.

#### THE NATIONAL ASPECT OF THE DISEASE:-

which we regard of prime importance. Does it, as a disease, received the attention which it merits? Do the Public, and the Medical Faculty fully appreciate the nature and extent of the disease? Regarding the former, it is quite evident that they do not realise the gravity of the condition. Possibly this may be due to the fact that, apart from the short acute stage of the disease there, is little to attract their attention

subjectively or objectively. Likewise they are quite ignorant of its infectious nature with its far reaching effects. We think however, that the Medical Faculty and the absence of Efficient legislation are more important factors.

It is comparatively recently that this disease has been brought home to the minds of Medical Men. With its pitfalls in diagnosis, small wonder that older practitioners failed to recognise it, let alone appreciate its important and far reaching sequelae. Curtis regards it "as an example of infection in Gynaecology, comparable to Typhoid importance in the realms of internal medicine". And that about sums up the importance of the question. Failure on the part of Medical Men to recognise it implies not only danger to the patient, but also the danger of the latter transmitting the disease inadvertently to other young children. In other words, such girls are 'Carriers' of the disease, and thus spread the disease further afield maintaining and even augmenting the incidence of Gonococcal Vulvo-Vaginitis. Which leads one to the question - is the disease on the increase or otherwise?. Since various authorities trace the chief source of infection in those cases to an infected parent, then it all depends on the question as to whether Gonococcal Infection on the whole is increased or otherwise. We are inclined to think that it is - factors such as the War, herding of people in large cities etc. all



have aided in increasing the incidence. And so it is quite logical, on that basis, to assume that Gonococcal Vulvo-Vaginitis is on the increase.

Again however, this is perhaps due to more accurate diagnosis plus more extensive facilities now available for better Medical Services.

Will the incidence of the disease ever be reduced to a very low percentage or even exterminated? Briefly putting it, much depends on better education of Doctors and the Public at large, plus a more efficient or even complete cure for the infection. We are dealing with the condition which can do untold harm be it socially, financially or physically.

And in conclusion one would like to suggest A FEW POINTS WHICH WOULD LEAD TO A MORE FAVOURABLE OUTLOOK.

(a) Make Gonorrhoea as a whole, a Notifiable disease. Such would have its drawbacks e.g. incur much expense to the State, but does not the present state of affairs warrant more drastic steps necessary? Why should Ophthalmia Neonatorum be a notifiable disease and yet Gonococcal Vulvo-Vaginitis is allowed to pass unchallenged? In its own way, the latter is every bit as dangerous as the former. True, it is more a problem of morbidity rather than mortality, but the gravity of the problem still remains, as has been previously pointed out when discussing Prognosis—immediate, and ultimate.



(b) "A tightening up" of the Standard of Cure.

Much could be attained in this direction by universal agreement on this point. As we stand at present, practically each and every author has his own ideas as to what comprises "Tests for Cure". Some are more rigid than others but at the best are far from satisfactory. The reason for this is difficult to understand. Perhaps we do not quite appreciate the actual "Relationship" between the Gonococci and the tissues. Thus, in the young female, this organism would appear to protect itself to a certain extent when placed in an unsuitable environment to existence. We know this to occur for example in Tuberculous Infection where the organism protects itself in a fatty waxy envelope which resists any attempt to kill the organism. It is maintained that when Gonococci are ingested by leucocytes, the latter do not kill every organism but simply renders those in question inert. Does this not suggest the intrinsic properties of self protection on the part of the Gonococci in unsuitable surroundings? Perhaps this explains the incidence of complications where the Blood Stream has been proved to be the root of infection (e.g. Gonococcal Arthritis). Thus the leucocytes, containing ingested organisms, wander back into the Blood Stream, and hence at some future time, when they die off, liberate those Gonococci still alive but inert, into the Blood Stream, since the life of a leucocyte is relatively short.

To return to the question of the tests for cure - One would personally enforce a longer period of observation since, in our present state of knowledge, we are so much in the dark on this point. This is practised by many authors, in infected adult females, and therefore, why should it not be carried out in greater measure in young children since they lack natural provocative measures (e.g. Menses) which aid in revealing latent foci of infection. Also the artificial provocative measures such as installation locally of irritant antiseptics should likewise be dispensed with.

From the little we have seen of it, we have been much impressed with the Gonococcal Complement Fixation Test as a measure to be employed in testing for cure. It is no more misleading than the Wassermann test is in the diagnosis of Syphilis, and intelligent interpretation of the results would prove extremely useful.

(c) The establishing of more facilities for examination of young females. - They should be examined for the possibility of this disease at birth and later on at Child Welfare Centres. Examination at birth would probably reduce the incidence by a small margin, but not very much since few cases occur after this fashion. We are of the opinion that Child Welfare Clinics should be made compulsory centres for the routine examination of young females, failing other suitable means for

periodic medical supervision. Associated with this ofcourse would be the necessity for raising the standard of knowledge pertaining to this disease among Doctors, Nurses etc. It should be impressed on them that Gonococcal Vulvo-Vaginitis is a free lance disease, and that it merits more care and skill on their part than it obtains at present.

(d) Ante-Natal Centres.

Within the last few years this has become more prominent but still demands more wide spread attention. Adequate steps taken at this stage, would help to reduce the incidence of the disease since, apart from the risk of acquiring it at birth, it is quite obvious how the mother might be the source of her daughter acquiring the disease e.g. clothes, sleeping together etc.

(e). More elaborate precautions taken when an outbreak is discovered, especially in the home. The other members of the household should be carefully examined, not only to determine the source but also to ascertain whether others, especially young girls, are infected.

Ofcourse here we are starting at the wrong end. Education for the Public would eliminate to a great extent the need for the above procedure. To attain this, one would recommend a better understanding between the Medical Profession and the Public - to

regard this disease as in unfortunate occurrence, but one which is fortunately curable in the majority of cases.

And thus the problem of Gonococcal Infection remains at the present day, We are dissatisfied with the various features throughout the disease - its doubtful reduction (or perhaps increase) in incidence; with the indecisive diagnostic methods employed at present; with the apparently futile and unsuccessful Therapeutic measures; and finally, probably the most important feature of all with the failure of all, concerned to realise its importance socially, economically, medically and from other point of view considered.

IRRIGATION WITH GENTIAN VIOLET

Foss<sup>111</sup> in 1920 used Methylene blue in glycerine in the treatment of adult female Gonococcal Infection, on the basis that this dye had a great affinity for Gonococci. Belonging to this series of dyes is Gentian Violet, which shows its powerful anti-septic properties in the treatment of other diseases—e.g. Impetigo. We employed it in a 3% solution;

## 142.a.

The remaining part of this Treatise is devoted to certain local therapeutic measures pertaining to "Irrigation", which were adopted and experimented with, in a fairly extensive series of cases.

logically the patients were much worse in fully 90% of cases on this line of treatment, which lasted on an average 4 weeks

IRRIGATION WITH GENTIAN VIOLET

Foss<sup>III</sup> in 1920 used Methylene blue in glycerine in the treatment of adult female Gonococcal Infection, on the basis that this dye had a great affinity for Gonococci. Belonging to this series of dyes is Gentian Violet, which shows its powerful antiseptic properties in the treatment of other diseases—e.g. Impetigo. We employed it in a 3% solution, and it was applied to the tissues by means of irrigation followed up by "Painting" the affected parts as thoroughly as possible.

CONCLUSIONS

One was satisfied, even although the case material available was limited, that Gentian Violet despite its vaunted antiseptic qualities was not so efficient as, say, Picric Acid or Potassium Permanganate. Actually, clinically and bacteriologically the patients were much worse in fully 90% of cases on this line of treatment, which lasted on an average 4 weeks



Another entirely new line of treatment was employed, in a small series of cases, which implies:-

#### THE APPLICATION OF SURFACE TENSION TO ANTISEPTIC THERAPY

Introduction As already emphasised, it is only in the very earliest stage of the disease one can hope to find Gonococci on the mucosal surface of the affected parts. Pathologically, we have shown that the organism tends to penetrate deeply, and ultimately is to be found in the submucosal region, crypts etc. Thus, access to the organism is rendered difficult and we must aim at promoting drainage and prevent the embedding of the Gonococcus in the deeper tissues. Histologically, the Vagina is bereft of complicated structure, there being no glands as compared with the adult, but in young girls the epithelium is of the columnar type which offers a poor defence. Thus we see Gonococci lying between and deep to those cells. If we have not been successful in preventing the ingress of the organisms to the deeper structures, we must attempt to bring the antiseptic into contact with the Gonococci situated thus. Hypertonic Saline promotes the shrivelling up of live tissue cells and should thus enable the antiseptic to pass deep into the tissues. Such is theoretically possible, but in practice it was found to be totally unsuccessful. Ten cases were tried out on this line of treatment with markedly disappointing results. Employing 5% Hypertonic Saline we noticed an increase in the

degree of positivity, and clinically the child suffered from gross discomfort combined with an appreciable increase in the severity of the discharge. Admittedly the series of cases treated thus was very limited, but the results were such as to warrant complete withdrawal of treatment.

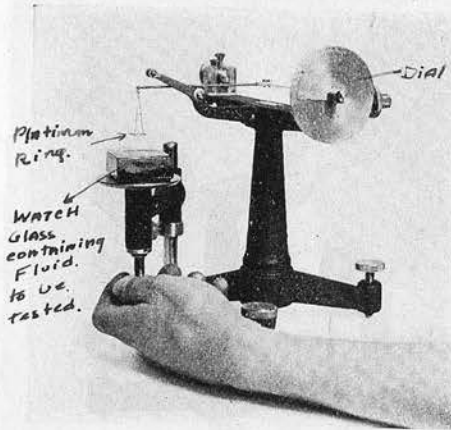
Recently in America and elsewhere, certain workers have been studying the principle of surface tension in relation to the bactericidal efficiency of antiseptics. On this basis they maintain that as a result of lowering surface tension the antiseptic was brought in closer contact with the Gonococcus. The problem is much more complex than this, however. Perhaps it would be better to explain a few facts pertaining to the Physics of surface tension.

Surface tension, as applied to liquids, is that property in virtue of which a liquid surface behaves as if it were a stretched elastic membrane. For example, a fine capillary tube inserted into a vessel containing water, results in the latter rushing up the tube to a level much above that of the water in the vessel. Likewise, large heavy clams may suspend themselves from filaments anchored to the under surface of water in aquaria.

Those examples show that the film of water molecules at the surface possess a remarkable tensile quality, surface energy, surface tension, or cohesion.

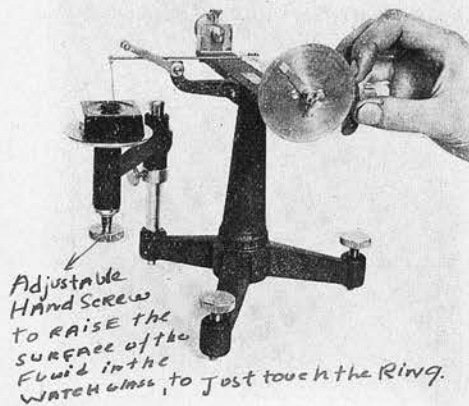
How can we measure the surface tension of various liquids? We regard Du Nouy's apparatus as very satisfactory. Herewith we append diagrams illustrating the mode of working of the apparatus:-

FIG. 8



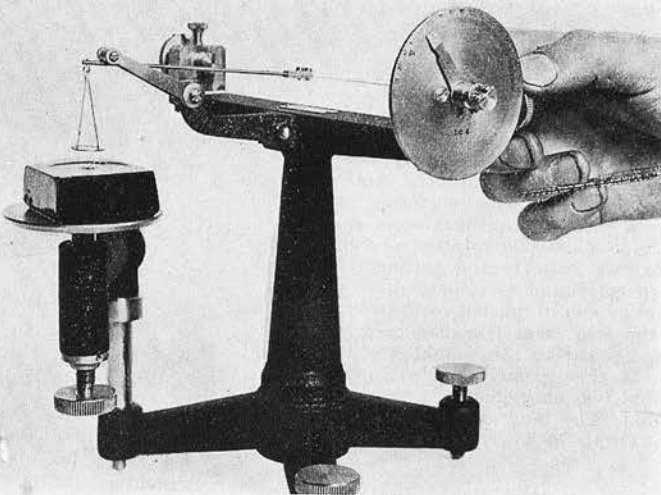
Preparing to make surface tension measurements. Note pointer on dial at zero, position of aluminum arm, and the fluid in container on adjustable disk.

FIG. 9



Appearance of fluid surface just before the break of the surface film. Note position of pointer, aluminum arm and the method of applying the torsion by means of the thumbscrew.

FIG. 10



Just after the surface film has broken. Note the position of aluminum arm and of pointer on dial.

One cubic centimetre of the liquid to be tested is placed in the watch glass. The force required to pull an platinum ring from the fluid surface is measured by that force exerting

tension on a wire - the amount of tension, and hence the value of surface tension is indicated on the graduated dial. The unit of measurement of surface tension is the DYNE which is an absolute unit of force, as opposed to a relative unit of force.

With this apparatus the following results have been obtained:- ordinary Potassium Permanganate solution from 1/1000 to 1/8000 has an S.T. of about 77 dynes per square centimetre. Zinc and Sodium Permanganate are approximately similar. Lecithin, with certain antiseptics, is an admirable substance for reducing surface tension e.g. Lecithin with Flavine gives an S.T. of 39 -40 dynes as opposed to about 50 in ordinary solution. Mercurochrome (aqueous) equals 77 approximately - in Lecithin solution about 40. (Lecithin however, is expensive in the pure state, and chemical interaction between it and the antiseptic is apt to occur). Practically all strengths of Argyrol can be brought down to a S.T. 30 - 31 by adding .2 c.c. n/5 Sodium Chloride. This mixture remains stable for 72 hours. N/10 Sodium Chloride gives an S.T. of 30, while n/80 is about 31 - 32. Unfortunately while it does not alter the Silver Salts, it destroys Permanganate.

Certain standard conditions are necessary before estimating accurately the surface tension of any liquid:-

(1) Clean apparatus e.g. the cleaner it is the nearer the true value one obtains of the surface tension.

(2) Time - It takes time for a new surface to attain its normal surface tension after having been disturbed, say, by a bubble of gas. After one minute an approximate value of the true surface tension is obtained.

(3) Temperature - Likewise, very important, since the higher the temperature the lower is the surface tension.

Within a body of fluid exists a cohesive or attractive force resulting in the molecules situated here, "neutralising" one another, since equal and opposite forces act in opposite directions. The surface layer however, is different. One component, that is, the force pulling downwards has no opposing upward force to stabilise the molecule. Thus a state of strain exists in the surface area which therefore possesses a greater number of molecules per unit area, since they are arranged in a definite manner as compared with those in the interior of the fluid,

Our aim is to employ this surface energy and such can be done by altering the surface tension. This occurs in normal physiological processes, in tissues abounding in surfaces, where one liquid phase subjoins another, similar or dissimilar phase. Alteration of the intrinsic energy of the liquid likewise alters the surface tension or energy.

This may be done Physically or Chemically. Regarding the former, we may ignore it, since raising of the



temperature is the only likely method, and it must be to such a degree as to be incompatible with life to produce sufficient lowering of the surface tension.

Organic substances with long "Carbon Chains" diminish the surface tension of water markedly, apart from the fact that they have a low surface tension themselves. In those "Carbon Chains" they have a radicle particular soluble in water - the Polar Radicle e.g. the Carboxyl Radicle - apart from which the remainder of the molecule is insoluble, or markedly less soluble, in the solvent.

Fatty Acids ( e.g. Palmitic ) lower the surface tension of water, because the unsatisfied valencies at the surface are satisfied by the soluble COOH group, while the insoluble Paraffin group remains out of the water, i.e. the fatty acid goes to the surface because that portion of the molecule which does not wet tends to leave the water but is anchored to the water by the Polar group. If there is sufficient of the substance present to cover the surface with a layer at least one molecule thick, then the surface tension will be decreased.

And finally, we may note that if the surface of a liquid is increased by the introduction of a finely divided solid, gas, or immiscible liquid, we may be able to remove completely the substance in solution.



THE BIO-PHYSICS OF SURFACE TENSION

The bacterial cell is surrounded by a membrane which is essential for the life of the organism e.g. by a process of diffusion, respiratory, nutritive, and waste products are excreted through this membrane. To kill an organism implies that the antiseptic must pass through this surrounding cell membrane. Such may imply the destruction of this membrane, which is semi-permeable, in the process of killing off the organism. So that a germicide must be in liquid form, to permit diffusion increase of which means increased bactericidal efficiency. If a substance which is capable of reducing surface tension is added to a germicidal solution both the velocity of disinfection and actual bactericidal power of that particular dilution of germicide may be increased markedly, despite the fact that the substance added has no toxic effect on the organism. This is due to the increased rate of diffusion of the germicide into the bacterial cell.

Substances reducing the surface tension of their solvents tend to collect about any surface or particle which may be in contact with the solution with i.e. mechanical adsorption which varies as the surface tension reducing properties of the solute. Two substances existing in the same solution and which are capable of reducing surface tension lead to the displacement of the weaker by the stronger one.

If a germicide itself is capable of reducing surface tension, its molecules, in the absence

of any solid particle suspended in it e.g. bacteria, would be adsorbed upon the surface of any bacteria which might be added to the solution. Thus, germicidal substances which reduce the surface tension of their solution actually become concentrated at the most effective point i.e. the surface of any organism. The concentration of such a germicide will therefore be very great in the immediate vicinity of any organism suspended in the solution. In addition, all other things being equal, plus the fact that under the circumstances the rate of diffusion of the germicide is increased into the cell (bacterial), a germicide which reduces surface tension will be much more efficacious than one which does not.

It is essential that in antiseptic therapy applied to the human live tissues, such substances must be capable of penetrating into the most remote crevice. In this, lies the great value of surface tension. Herewith is appended a few diagrams illustrating the value of fluids with low surface tension:-

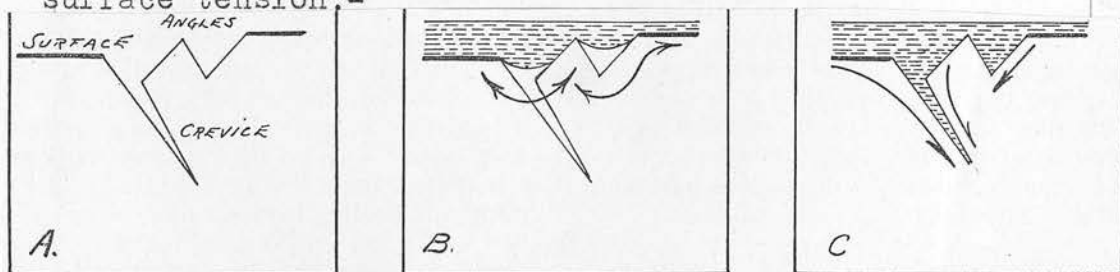


Fig. 7. Penetration by fluids of low surface tension. A, Microscopic irregularities in surface. B, The same surface covered by a fluid of high surface tension. The strong retaining surface film prevents its extension into the

depths of angles and crevices. C, The same surface covered by a fluid of low surface tension. The readily extensible surface film allows a labile process to flow into each irregularity in surface.

from which it is perfectly obvious that substances with lowered surface tension are capable of greater penetration.

Let us now apply the above facts to our problem. It is likely that inorganic antiseptics are of little value if any at all. This may be due to two factors (a) the antiseptic strength essential for killing off the organism is much too near that which is liable to impair the tissues; (b) the effect of the antiseptic is liable to be wiped out by the tissues surrounding the organism e.g. a drop of Potassium Permanganate placed in the palm of the hand soon loses its colour. This is due to the tissue oxidising the Potassium Permanganate presumably, before the latter has reached the organism and thus the antiseptic effect is lost.

Which brings us to the point - what factors are essential to constitute an ideal antiseptic under the conditions in point? We would suggest that it must have the following properties:-

- (1) Great germicidal power.
- (2) Relatively stable.
- (3) Non toxic.
- (4) Non irritant.
- (5) Odourless.
- (6) It must not stain.
- (7) HIGHLY PENETRATING.

One cannot estimate the efficiency of an antiseptic "in vitro" as compared with "in vivo", since debris, tissue salts, mucous etc., exert a detrimental effect on the antiseptic in question.

The Inorganic antiseptics have little

power, if any at all, of reducing surface tension.

Now, if one employs such an antiseptic as Potassium Permanganate, in a suitable strength, in a one per cent Sodium Stearate solution - the latter with a view to lowering surface tension - it is very doubtful if the antiseptic value of Potassium Permanganate is obtained. The Sodium Stearate, with its power of lowering surface tension, tends to aggregate in a definite molecular form around the bacteria and thus the antiseptic which, as we have already pointed out has a very low potential power of lowering surface tension, is thus probably prevented mechanically from exerting its antiseptic action. And since Sodium Stearate has practically no lethal effect on the organism, small wonder one obtains discouraging results with this line of therapy.

Certain types of Organic salts as we have seen have a long "Carbon Chain" and therefore, have good lowering-surface-tension properties i.e. congregate at the surface of the liquid. In this group we must mention particularly HEXYLRESORCINOL which possesses 70 times the germicidal efficiency of Phenol. Hexylresorcinol in addition, possesses a powerful antiseptic action due to the "Phenol radicle". Such has an obvious advantage, since the two important factors are present in the one and same substance. If we were to employ two substances together (a) to promote lowering of the surface tension, (b) an antiseptic, and if the latter possessed any lowering-surface-tension property at all, the stronger of the two would oust the weaker - most

likely the antiseptic. Thus, we would not be any further forward from the lethal point of view as we were in employing Inorganic antiseptics dissolved in distilled water.

In addition to the above explanation regarding the failure of Potassium Permanganate, a further explanation can be put forward:- the bacteria are surrounded by a semi-permeable membrane, and it is just possible that the size of the molecule in many of the antiseptics, such as Potassium Permanganate, employed was too large to diffuse through the membrane. Moreover, the antiseptics brought in contact with the affected tissues by means of irrigation, were only allowed to remain for a relatively short space of time. Again there may have been interaction between the antiseptic and the tissues (salts e.g. Chlorides), resulting in the formation of an innocuous substance. And still another point - there may have existed an incompatible boundary between the antiseptic and the cell membrane of the organism. Such for example, may take the form of Dirt, Debris, etc. the importance of which is perfectly obvious.

The reaction between the organism and the antiseptic is in the nature of a chemical one, between the cell protoplasm and the disinfectant. The disinfection of an organism is an orderly time process (i.e. not a haphazard one) or, if we express it in another way, a so-called uni-molecular reaction.



just as occurs in the Hydrolysis of cane sugar.

Around the organism is this cell membrane which must be penetrated before the antiseptic can exert its action. If the surface tension is lowered, both Osmosis and Diffusion are accelerated. Therefore, that organism receives a greater concentration of the antiseptic in a given time i.e. adsorption on the surface of the organism, and therefore greater concentration, and therefore increased Osmosis and Diffusion-all leading to a still greater concentration. Moreover, bacteria thus adsorbing antiseptics which reduce surface tension, result in an actual concentration of the antiseptic in question on the surface of the organism, so that in the case of 1/1000 of such an antiseptic, the concentration on the surface of the organism i.e. on the most effective part will be actually greater than 1/1000.

#### Acyl and Alkyl derivatives of

Resorcinol all lower surface tension. In this group, from the simplest chemical combination up to the hexyl and hexyllyl combinations, the increasing bactericidal power varies directly as their ability to lower surface tension. (Frobisher - Journal Infect. Diseases 1926, 38, 66).

Hexylresorcinol is practically as powerful in lowering the surface tension as Sodium Oleate. It has also a very high bactericidal power. A germicide such as Phenol, which failed to destroy B.Typhosus did so, if a substance which lowered surface



tension was added - the latter having no bactericidal power whatsoever. Examples of such substances are Sodium Oleate and Ethyl Acetate. Excess of either of those substances renders inert germicidal dilutions which acted in combination with a less percentage of either of the two. Excess of either of the latter is adsorbed on the surface of the organism, thus forming a protective film for the organism in question and therefore, preventing the germicide from obtaining contact with the organism. Hexylresorcinol lowers the surface tension of Urine and imparts germicidal action to the urine. If it is given however with copious draughts of water or with Diuretics, the surface tension rises and consequently the germicidal power disappears. Diuresis causes a rising of the surface tension. Therefore, when giving hexylresorcinol excess of fluid intake must be avoided.

Hexylresorcinol, ~~XXXX~~ can lower the surface tension of pure water from 77 dynes per sq. cm. to 34; with glycerine the surface tension is lowered only to 67 dynes per sq. cm. Glycerine retards disinfection, since the surface tension is relatively higher as compared with water, but there is a greater concentration of hexylresorcinol within the glycerine. Water together with glycerine raises the surface tension, but if the glycerine contains hexylresorcinol, addition of water to that mixture lowers the surface tension i.e. a greater germicidal action. Therefore, water in this mixture lowers the surface tension while glycerine acts

by ensuring a perfect solution of hexylresorcinol.

In choosing an antiseptic we must allow for the following effects on the efficiency of that antiseptic from such points of view as concentration for example (a) dilution when coming in contact with moist surfaces and (b) organic matter both of which reduce the potency of the antiseptic to a varying extent. Fortunately however, in the treatment of such a chronic condition as Gonococcal Vulvo-Vaginitis we have a more or less standard organic mixture i.e. mucous, cellular debris etc.. One must accordingly test the antiseptic in question against those two factors and take them into consideration, otherwise it is perfectly obvious the efficiency of the surface-tension-lowering antiseptic mixture will be markedly impaired.

#### SUMMARY

We employ surface tension in antiseptic therapy for many reasons. To mention a few:-

(1) Surface tension plays a major role in disinfection by chemical means.

(2) On account of its penetrating powers—for example, a mixture such as Sodium Stearate combined with any of the commoner dyes, tends to flow readily into the depths of a microscopic surface showing irregularities which may harbour bacteria. This ofcourse, was an observation made "in vitro" and, although it could not be proved definitely "in vivo", it is quite logical to

assume that such could happen.

(3) Under equal conditions, a germicide capable of lowering the surface tension of water is more efficient than one which does not, because (a) there is a greater extensibility of the fluid film of low surface tension and the germicidal solution is therefore, more liable to penetrate microscopic inequalities in the surface normally inaccessible to fluids with a high surface tension. (b) Germicides which lower surface tension are adsorbed by particles in suspension e.g. bacteria. The germicide concentrates at the most effective point i.e. on the surface. (c) Diffusion of the germicide through the cell membrane of the organism is accelerated as the surface tension is lowered, so that the bactericidal efficiency varies inversely as the surface tension.

### CONCLUSIONS

We have emphasised repeatedly the failure of "irrigation" with inorganic antiseptics. We have pointed out the histological and pathological difficulties which must be overcome before the Gonococci can be killed off. The question now arises—can this new form of therapy deal with this difficult problem?

It is to be admitted that our results would not seem to justify our optimism. A series of cases were treated on the following preparation:-

1% Sodium Stearate combined with 1/5000 Potassium Permanganate; the patient was irrigated twice daily with this preparation and the results were as follows:-

- (a) the Severity of the infection remained I.S.Q. or showed a slight improvement in a little over 50% of cases.
- (b) no complications developed during this period.
- (c) the child did not object to the treatment i.e. no discomfort, irritation etc.
- (d) the period of 7 weeks during which the treatment was carried out did not retard the ultimate progress of the case. So that the "experiment" was not a failure, but neither was it a success. Obviously however the results should have been infinitely better, if surface tension was to act as it should theoretically. There must have been a reason!

We arrived at certain conclusions as to the possible explanation of our failure:-

- (1) Were we employing the proper strength of Sodium Stearate? If the concentration was too high, as Frobisher has shown the excessive adsorption of the Sodium Stearate by the organism would form a barrier to the ingress of the antiseptic. And since the Sodium Stearate has no antiseptic value in itself, this may have been a possible explanation.
- (2) The "parts" involved were merely irrigated with the "mixture". In view of the fact that it may take a little time for the surface tension to adjust itself, probably we did not allow sufficient time to act.

- (3) Possibly there was some chemical interaction between the Sodium Stearate and the antiseptic. The former was chosen solely on this account, in preference to Sodium Oleate since the latter is more easily "chemically" decomposed. We observed that even then there was a slight suspicion of Double Decomposition shortly after the preparation had been made up.
- (4) Debris, mucous etc. inhibit the action of an antiseptic especially of the inorganic type as alluded to.
- (5) Dirt, as we have seen, tends to maintain a higher surface tension. In other words the cleaner the tissues implicated the lower the surface tension obtained.
- (6) Many of the children were on "Alkaline" treatment which was administered orally (this will be referred to later).
- (7) We did not attempt to vary the percentage of the antiseptic or stearate in the mixture i.e. we did not treat each and every case on its own merits.
- (8) The patient drank copiously of water as part of the treatment.

From the above then we cannot condemn surface tension treatment. We must admit that it was not given a fair trial. We are not violating the Physiological functioning of the body with this line of treatment, since much of the former is based on the mechanism of surface tension e.g. during Secretory activity. So that this method is based on sound



Physiological Principles with a full view of the bacteriological and pathological pictures.

From all that has been said, it is obvious that the ideal object is to obtain a preparation which will lower surface tension and be bactericidal i.e. the two essentials present in the one substance. Failing that, and in view of the fact that tissue material impairs the action of inorganic antiseptics, it would seem rational that the bringing of the organism within reach of the antiseptic by means of lowering the surface tension, is the proper procedure. Also, since we have found that the incorporating of those two substances in the one "irrigation" is unsuccessful, we suggest that the affected parts having been previously thoroughly cleaned, Sodium Stearate should first be employed, followed shortly afterwards by the antiseptic. One possible objection to this line of procedure is the subjecting of the tissues to a "double irrigation" which might lead to further chemical and mechanical irritation.

The coexistence of the bactericidal and the surface-tension-lowering properties of hexylresorcinol has already been referred to. This implies (a) increased speed of disinfection, (b) increased effectiveness of a given dilution, and (c) increased powers of penetration.

We have already mentioned the question of alkalinity as applied to surface tension. In a



normal healthy person hexylresorcinol retains its germicidal properties when the urine has become alkaline which ofcourse, is a normal physiological phenomenon. The administration of certain alkalis, especially Sodium Bicarbonate, completely robs the urine containing hexylresorcinol of its bactericidal properties, because alkalis raise the surface tension of the urine considerably. So that the detrimental effect of Sodium Bicarbonate has nothing to do with alkalinity but everything to do with raising the surface tension which, as we have already seen, decreases the germicidal powers of hexylresorcinol.

The effect of intake of large amount of fluid or what amounts to the same thing, the administration of Diuretics acts similarly in that it raises the surface tension of the urine. This ofcourse defeats the very object of both the local and internal antiseptic (hexylresorcinol) treatment of chronic urinary Tract infections.

From which we conclude, the administration of hexylresorcinol necessitates the minimising of fluid intake and likewise the administration of alkalis, especially Sodium Bicarbonate.

Glycerine has been widely used as a basis for the application of such antiseptics as Picric Acid in irrigation therapy. It is highly hygroscopic, and for this reason is employed in Culture Media to prevent them from drying. Following irrigation, it

has been pointed out that the essential feature is to keep the affected parts as dry as possible e.g. by means of Insufflation. Therefore, it would seem the using of glycerine is antagonistic to drying in view of its hygroscopic property. Moreover, it is practically certain that the attempted swabbing following irrigation to dry the parts, cannot completely remove all the antiseptic in contact with the tissues. Such ofcourse implies that glycerine is left in the more inaccessible regions of the affected areas and apart from the maintenace of moisture, it is just possible it may act as an ideal pabulum for the Gonococcus to thrive on.

Hexylresorcinol dissolves very well in glycerine and, in view of what we have already said, it would seem that glycerine should not be employed. Moreover, the latter's surface tension is reduced only very slightly as compared with water, by hexylresorcinol. However, in combination with the latter substance, glycerine is suitable since the presence of water in this "mixture" releases the surface tension depressant properties of hexylresorcinol. The shortcomings of glycerine are compensated for amply, by the fact that it acts as an excellent solvent for hexylresorcinol which on account of its eminently suitable properties would seem to be an ideal preparation in treatment of Gonococcal Vulvo-Vaginitis. Experimental evidence has shown that it can be used in dilution to 1/5 with satisfactory results as a Gonococcocide.

Such could be employed in this given dilution as an "irrigation", It has been found as such to be very suitable in infections of the Urethra, Bladder, and Renal Pelvic conditions. But, since surface tension "takes time", we are of the opinion that it would give more satisfactory results were the solution employed in the form of a Soak or Tampon, where it could be given in full strength without any toxic effects.

### SUMMARY

We would suggest that hexylresorcinol (1 mgm.), plus 70 parts of water, plus 30 parts of glycerine (i.e. S.T. 37), would be a satisfactory preparation, or replacement of the glycerine - since it is hygroscopic - by 20 parts of alcohol, and therefore 80 parts of water, would in all probability be equally satisfactory. Furthermore, this form of treatment should be persevered with. And finally, if the results were a little disappointing, the percentage of hexylresorcinol could be slightly modified thereby, possibly making a change for the better. In other words, judge each case on its own merits, and administer this line of therapy accordingly.

oooooooo00000000oooooooo.

REFERENCES.

1. Suchard, Rev de la Suisse, Romande, 1877. Vol.VII.  
(675).
2. De Minine, Journal de Med. de Paris, June 8th.1895
3. Veil & Bayon, Semaine Med. 1904.
4. Hamilton, Jour. Americ. Med. Assoc. 1910 LIV.(1196)
5. Lees, Edin. Med. Jour. May 1928 (70)
6. Brown, Brit. Jour. of Venereal Diseases 1930 (285)
7. Buckley-Sharpe, Brit. Jour. of Veneral Diseases  
1930 (301).
8. Tod, Brit. Jour. of Veneral Diseases Vol.III.  
1927 (113).
9. Brunet, "Gonococcal Cervo - Vaginitis" in  
children - Bellvue Hospital Magazine May 1933.
10. Reith Fraser, Brit. Jour. Venereal Diseases  
Oct 1925 No.4. Vol.I (268).
11. Williams, Americ. Jour. of Obstetrics and "Gynaec"  
Vol.XXI. 1928 (861).
12. Titus & Notes, Arch. Pediate 47: 1, 58. Jan.1930.
13. Kurzwel & Saxl, Archives of Pediatrics XLII  
1925 (202).
14. Atkinson, Americ. Jour. Medical Science, 1898  
LXXV. (444).
15. Skutsch, Inaug. Didd, Jena 1891.
16. Cotton, Arch. f. Pediate 1905 XXI. (100).
17. Plomley, Australian Med. Gazette 1906 (455).
18. Hurdon, "Kelly & Noble" - Gynae & Surg. 1907, 1.  
(811).
19. Pollock, Americ. Jour. Derm. & Genito - Urin. Dis.  
1909 (289).
20. Morrow & Bridgeman, Jour. Americ. Med. Assoc. 912  
Vol. LVIII. (1564).
21. Watson, "Gonorrhoea and its Complications",  
London 1914 (285).
22. Kidd & Simpson, "Common Infections of the Female  
Urethra and Cervix" 1924 (97).
23. Pott, "Jahrb. f. Kinderheilk, 1883 XLX.

24. Kimball, Med. Rec. 1903 LXIV. (761).
25. Reith Fraser, Brit. Jour. Venereal Diseases 1926 11. (8).
26. Abel, Discussion Venereal Diseases Inst. March 15th. 1922.
27. Dukelski, Jahrb. f. Kinderheilk 1904 LIX (397).
28. Spaulding, Americ Jour. Diseases of Children 1932, V (248).
29. Mickelberg, Jour. Americ. Med. Assoc. 1921 LXXVI. (164).
30. Smith, Amer. Jour. Diseases of Children, Vol.V. No.4., Vol. VII. No. 3.
31. Fischer, "Diseases of Infancy in Childhood".
32. Sherber, Handb. der. Geschlechtskrankheiten, Vol.1. (153).
33. Engering, "Zeit. f. Hyg. u. Infektion Skrank" Sept. 1923 (314).
34. Von Pourtales, "Archive of Pediatrics" XLIX 1932 (123).
35. Taussig, Americ. Jour. Med. Sc. 1914. CXLV111.(480)
36. Norris, Jour. Americ. Med. Assoc. 1915 LXV (327).
37. Morton, "Genito - Urinary Diseases and Syphilis" 1919 (24).
38. Trenwith, New York Med. Jour. 1906 (240).
39. Reith Fraser, South Africa Med. Jour. Oct. 25th. 1924.
40. Paine, Boston Med. & Sug. Jour. CLXXXV 1921 (715).
41. Hiss, Americ. Jour. Diseases of Children XII. 1916 (466).
42. Rubin and Leopold, Americ. Jour. Diseases of Children V.1913 (58).
44. Luys, Gonorrhoea and its complications "Foerster's Translation", 2nd. edit. Bailliere, Tindall and Cox.
43. Finger, "Pathological Anatomy of Gonorrhoea in Man", arch. f. Derm. u. Syph., Eng. 1.
45. Jadassohn, "Uber die Gon. der paraurethralen und praputialen Drusengange", Deut. Med. Woch.



46. Wertheim, Arch.f. Gynak., Vol.41.No. 1.
47. Schridde, "Histological Diagnosis of Gonococcal Salpingitis", Deut. med. woch.,(1251).
48. Hamilton, Venereal Diseases Information Vlll. 1927 (86).
49. Baer, Jour. Infec. Diseases 1904 1, (313).
50. Anderson, Schultz and Stein, Americ. Jour. Infec. Diseases 1923 Vol. XXXll. (444).
51. Pribram & Jonas, Proc. Soc. Expt. Biolog. & Med. 25: 627 May 1928.
52. Clauberg, Venereal Diseases Infor. Xl. 1930 (274).
53. Muller and Oppenheimer, "Demonstration of Antibodies in the Serum of cases of Gonococcal Arthritis by means of the Complement Deviation Method". Wien. klin. Wochenscher (894).
54. Osmond & Oliver "Complement - Fixation in Gonorrhoea: a Series of 1000 Tests". Lancet, June 10th. 1922 (1143).
55. Torry and Buckell, "Jour. Immunology" July 1922 Vll. (305).
56. Pearce, "Comparison of Adult and Infant Type of Gonococci", Jour. Exp.Med., Lancaster, Apr.,Vol. 21 No. 4. (289).
57. Magner, "The Complement Fixation Test in Gonorrhoea", Lancet 1920. Vo. 2.(123).
58. Dooley, Amer. Jour. Diseases of Children 1931 (1086).
59. Matthisohn, Ard. f. Derma. u. Syph. 1913, 116:817.
60. Wolffenstein, " " " " " 1914,120:177.
61. Pontopiddan, Dermat. Wehnscher, 1915, 61: 1077
62. Von Buschke and Gumpert, Med. Welt. 1927 1:695.
63. Koplik, Americ Jour. Obstetrics and Gynaec 1913, 68: (600).
64. Kjellberg Romanus, Dermat Wehnscher. 1917,(64)
65. Lode, Deut. Med. Woch. 1909 XLlV (714)
66. Schulz, Jour. Americ. Med. Assoc. 1920 LXXV:(512).
67. Maggiore, Pediatria, Naples - May 1919 (257).



68. Simmins, Lancet 1922, 11. (744).
69. Harrison, St. Thomas Hospital Gazette 1923, XXIX (310)
70. Bland, New York Med. Jour. 20th. March 1920.
71. Patschke, Deut. Med. Woch. 1921, XLVII. (44).
72. Abraham, "Lectures on Gonorrhoea in Women and Children", London 1924 (10).
73. Titus and Notes, "Arch. of Pediatrics". Vol. I No. 4 Apr. 1933.
74. Schaffer, "Uber Desinfektionsversuche an Gonokokken", Fortschr. d. Med. No. 5. 1896.
75. Finger, Ghon and Schlagenhauser, "Biology of the Gonococcus and Pathological Anatomy of Gonorrhoea" Arch. f. Derm. u. Syph. Bd. 28 (3).
76. Stein, "Surg. Gynae., and Obstetrics" 1923 XXXVI. (43).
77. Turner, "Treatment of Gonorrhoea in Women" Texas State Jour. of Med. Fortworth Vol. 15. No. 7. (253).
78. Schwartz and Davies, "Testing of Germicidal Substances against the Gonococcus". Jour. Infect. Diseases Chicago Vol. 27. No. 6. (391).
79. Maheu, "Bul de la Soc. Med. des hopit. Paris Vol. 41. No. 32 (1178).
80. Harrison, Text Book of Venereal Diseases,
81. Cole & Meakins, "Treatment of Gonorrhoeal Arthritis by Vaccines" Johns Hopkins Hospl. Bull., Vol. 18, No. 195 (223).
82. MacLachlan, "Thomson's Gonorrhoea" 1923 (345).
83. Thomson, "Text Book Gonorrhoea" (335).
84. Corbus and O'Connor, Venereal Diseases Information XI 1930 (486)
85. Hamilton, "Vulvo-Vaginitis" Jour. Infect. Diseases. Vol. V. (133) 1908.
86. Churchill and Soper, Jour. Americ. Med. Assoc. 1908 1. (744)
87. Lees, "Thomson's Gonorrhoea" 1923 (473).
88. Daken, "Munch Med. Woch. 1920 LXVII (1172).
89. Butler and Long, Jour. Americ. Med. Assoc. 1918 Vol. 1. (744)

90. Eyre & Stewart, "Lancet" 1909 Vol.11. (76).
91. Hamilton & Cooke, Jour. Infect. Diseases 1908 Vol. V. (153).
92. Whitehouse, "The Practitioner" 1910 Vol. 1.(499).
93. Schmitt, "Munch Med. Woch" 1911 LVIII. No. 51.
94. Fitzgibbon, "Brit. Med. Jour." 1913 Vol.1.(716).
95. Frassi, "Rivista di. clin. Pediate". 1921, XIX (290).
96. Bruck, "Deut. Med. Woch. 1909 XXXV (470).
97. Sommer "Munch Med. Woch." 1912 LX (1185).
98. Sauvage, "Le Bull Med."1913.
99. Hamburger, "Deut. Med. Woch", 1914 XL.No.15.
100. Glasgow Med. Jour. 1913 11. (84).
101. Americ. Jour. Diseases of Children, 1913 V.(313).
102. Sullivan & Spalding, Jour. Americ. Med. Assoc. 1916 LXVI. (95).
103. Herrold & Hoffmann, "Biologic Therapy of Gonococcal Vulvo-Vaginitis" Venereal Diseases Information 1930 Vol. 1 (397).
104. Courtin, "Med.Welt"., Berlin 1930 IV. (637).
105. Kaumheimer, Munch. Med Woch. May 3rd. 1910.
106. Valentin, Deut. Med. Woch. 1921 XLVII (628).
107. Vogt, Venereal Diseases Information VIII. 1927 (97).
108. Galvagno, Archiv. di. Patobe. Clin. Infant., 1904 Nos. 3, 4, Vol.XI.,(73).
109. Anwyl Davies, Brit. Jour. Venereal Diseases 1930 (306)
110. MacNicol, Quoted by Tod, Brit. Jour. Venereal Diseases 1927, No.2. Vol.III.(113).
111. "Treatment of Gonorrhoea in Women". Brit. Med. Jour. 1920, Vol.1. No. 3091 (434).
112. Nabarro, "British Jour. Venereal Diseases 1930" page 305